EXHIBIT 19

Redacted Version of Document to be Sealed

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF MICHIGAN
SOUTHERN DIVISION

ELNORA CARTHAN, et al., Plaintiffs,	
v.	Case No. 5:16-cv-10444-JEK-MKM
RICK SNYDER, et al., Defendants.	Hon. Judith E. Levy Magistrate Judge Mona K. Majzoub

DECLARATION OF STACEY M. BENSON

My name is Stacey M. Benson. I provide the attached report in support of the VNA Defendants' Opposition to the Plaintiffs' Motion for Class Certification. I declare under the penalties of perjury that the statements made in my report are true and accurate to the best of my information and knowledge.

Stacey M. Benson, PhD

Date: January 4, 2021

Expert Report of Stacey M. Benson, PhD

In Re Elnora Carthan, et al. v. Rick Snyder, et al., Case No. 5:16-cv-10444-JEL-MKM

January 4, 2021

Cardno ChemRisk

Prepared for Dave Rogers
Campbell Conroy & O'Neil
1 Constitution Wharf, Suite 310
Boston MA 02129

Date January 4, 2021

Prepared by:

Stacey M. Benson, PhD
Cardno ChemRisk
20 Stanwix Street
Suite 505
Pittsburgh, PA 15222

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EXPERIENCE AND QUALIFICATIONS

I am an epidemiologist with over 15 years of professional experience conducting, analyzing, and interpreting scientific data using well-accepted scientific methodology. My areas of expertise include environmental epidemiology, occupational epidemiology, respiratory protection, and clinical research. I have a bachelor's degree in Physics from St. Lawrence University, a master's degree in exercise physiology from The University of Pittsburgh, and a doctoral degree in Epidemiology from The University of Pittsburgh.

As a graduate student, my research focused on exposures to industrial and aviation emissions of lead and their contribution to childhood blood lead levels. My research also included evaluations of exposures to air pollution, specifically particulate matter, and associations with mortality and morbidity endpoints. Over the course of my career as a scientist, I have used epidemiological and geospatial techniques to evaluate environmental exposures to chemicals and health outcomes in children and adults. Example publications include Benson et al. (2018); Benson et al. (2017); Benson et al. (2013); Brink et al. (2016); Brink et al. (2014); Marsh et al. (2017); Talbott et al. (2014); Talbott et al. (2013). I have also presented my research at various national and international conferences on topics that assessed health outcomes and environmental exposure various chemicals including vinyl chloride, asbestos, 4-methylchclohexanemethanol, ambient air pollution, particulate matter, and lead.

Prior to my work with Cardno ChemRisk, I was employed as an Associate Service Fellow at the National Institute for Occupational Safety and Health in their National Personal Protective Technology Laboratory. I was responsible for conducting clinical research and recording anthropometric data so that I could develop the current standard ISO headforms that are used in the development of personal protective equipment for the head and face. I have also held positions as a special lecturer and laboratory technician at Carnegie Mellon University in their physics department and as an adjunct Instructor at Point Park University.

For the past five years, I have worked closely with clients to submit applications to the FDA for authorization for their consumer products, which serve as an alternative source of nicotine for combustible cigarette consumers. As the clinical lead, I have been responsible for designing and overseeing numerous clinical studies including but not limited to pharmacokinetic studies, behavioral surveys, and biomonitoring studies to evaluate the overall impact of new tobacco products on population health. I have conducted numerous literature reviews, covering the key topic areas associated with these submissions: clinical health, abuse liability and pharmacokinetic, initiation, cessation, topography, human factors, consumer perception, and population modeling. In addition, I worked with my colleagues to evaluate the findings from toxicological, clinical studies, and benchtop testing to understand the risks associated with the use of these products for the individual using them and for the population as a whole, including non-users of these products.

I currently serve as a Senior Managing Health Scientist at Cardno ChemRisk, a global scientific consulting firm specializing in, among other areas, product health and safety. Cardno ChemRisk is a consulting firm that provides scientific advice to the government, corporations, law firms and various scientific/professional organizations. I have published over 35 scientific articles, presented 28 papers at both national and international conferences, and have been cited in the scientific literature over 550 times.

I have testified as an expert in deposition in one case, which will go to trial in January of 2021: Certain Tobacco Heating Articles and Components Thereof, Investigation No. 337-TA-1199.

My curriculum vitae, dated September 28, 2020, which presents my training, qualifications, and experience, is included in Appendix A.

My time spent in reviewing the materials as well as for report, deposition, and trial preparation will be billed at a rate of $350 per hour.

1 SUMMARY OF OPINIONS

Based on my background, education, and experience as an epidemiologist and my review of the materials identified herein, I hold the following opinions to a reasonable degree of scientific certainty. These opinions are based on information available to me as of the date of this report and I reserve the right to supplement these opinions if or when additional information becomes available.

2.1 Lead is Commonly Present in the Environment and Results in Exposures that Influence Blood Lead Levels in Human Populations.

2.2 Seasonal Fluctuations in Blood Lead Levels are Common and Not Unique to Flint, Michigan.

2.3 There are Known Non-Chemical and Chemical Factors Other than Lead that Impact Intellectual Development in Children.

2.4 Based on the Scientific Evidence to Date, Blood Lead Levels Less than 5 µg/dL are Not Causally Associated with Decrements in Cognitive Abilities in Children.

2.5 There is No Scientific Evidence that Low Prenatal Lead Exposure (measured at concentrations ≤ 5 µg/dL) Leads to a Reduction in IQ.

2.6 No Causal Associations can be Established Between Maternal or Umbilical Cord Blood Lead Levels ≤ 5 µg/dL and Birth Weight, Gestational Age (or Preterm Birth), and Small for Gestational Age.

2.7 There is No Scientific Evidence that Low Blood Lead Levels (Measured as ≤ 5 µg/dL) Lead to Reduced Cognitive Function in Adulthood

2.8 There is No Scientific Evidence that Low Blood Lead Levels (Measured as ≤ 5 µg/dL) are Associated with Criminality or Delinquency

2.9 Contrary to the Opinions Expressed by Dr. Howard Hu There is Insufficient Scientific Evidence to Draw A Causal Connection Between Low Level Lead Exposure (< 5 µg/dL) and IQ Decrements in Children

2 OPINIONS AND BASES FOR THE OPINIONS

2.1 LEAD IS COMMONLY PRESENT IN THE ENVIRONMENT AND RESULTS IN EXPOSURES THAT INFLUENCE BLOOD LEAD LEVELS IN HUMAN POPULATIONS.

Lead has been used since ancient times for a myriad of purposes: make-up, pigments in paints, wine preservative, coins, and inexpensive cups, plates, and pitchers. Lead mining and smelting began as soon as the US colonies were settled, with initiation in Virginia as early as 1621 (Lewis 1985). Due to poor smelting practices during the Industrial Revolution, lead ore dusts and lead smelter fume were released into the atmosphere. These practices continued until the early 1900s, when lead ore started to become scarce and recovery efforts of smelting fumes improved (Murozumi et al. 1969). Then, in the 1920s, tetraethyl lead was developed and included as an additive for gasoline for use in piston driven engines. Efforts to remove lead from gasoline were not initiated until the 1950s and not fully implemented until the 1980s (Needleman 2000). Assessments of Northern Greenland snow layers demonstrate that lead and other minerals have been deposited at levels that correlate with these industrial activities (see **Figure 1**) (Murozumi et al. 1969). By 1980, the US was consuming 1.3 million tons of lead per year, and due to its presence in the air, drinking water, and food, every person in the US was considered exposed (NAS 1980).

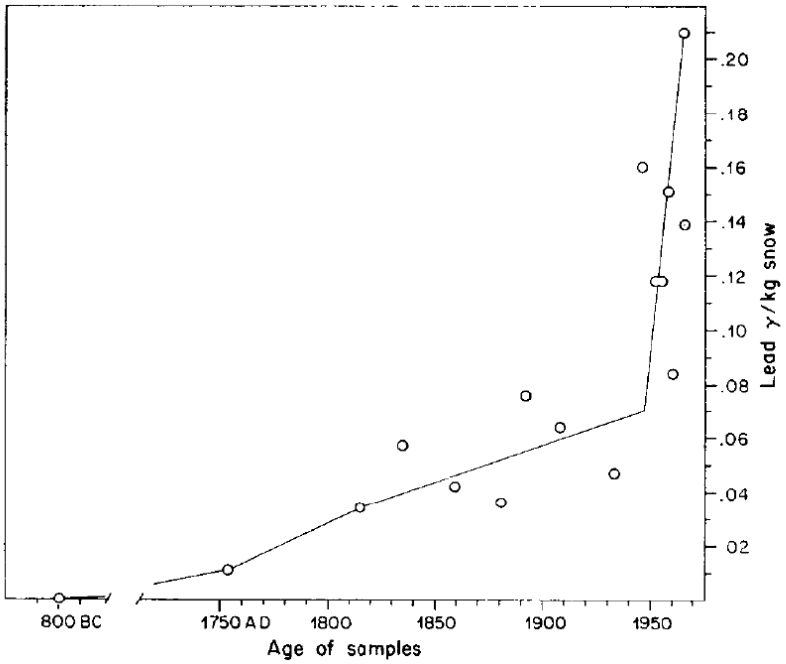

Figure 1. Increase of industrial lead pollution in Camp Century snow with time since 800 BC (Murozumi et al. 1969, p 196; Figure 6, p. 1285)

Due to concern about the pervasiveness of lead in the environment, many regulations were implemented, beginning in the 1970s, to reduce the use of lead in consumer products and to minimize emissions. Between the early 1970s and 1986, lead in gasoline was reduced from 1 g per gallon to 0.1 g per gallon (EPA 2000). Industrial lead emissions were reduced by 99.7%

between 1970 and 2014 (EPA 2018). Lead-based paint was prohibited from use in residential structures starting in 1978 (CDC 2020). Subsequently, lead-based pesticides and lead solder on food cans were banned completely in 1988 and 1995, respectively (EPA 2004; FDA 1995).

Environmental lead is found primarily in sediment and soil and does not leach appreciably into subsoil or groundwater (ATSDR 2007). Concerns remain regarding exposure to lead, especially in children, due to residual sources in the environment. The primary sources of lead exposure to children are contaminated soil and lead paint. Even though lead in residential paint has been banned, over 90% of the homes in Flint were built prior to 1980 (U.S. Census Bureau 2018). Flaking and chipping paint contribute to exterior contamination of soils surrounding the home and to lead dust generation within the home. Other potential sources of lead exposure include water, food sources, and toys (Dignam et al. 2019).

Since the 1970s, the Centers for Disease Control and Prevention (CDC) has worked with state and local health departments to develop lead monitoring and lead poisoning prevention programs. These programs are designed to monitor child blood lead levels (BLL) and to provide parental education, counseling, and home visits to remediate potential environmental lead exposures to children (Ettinger et al. 2019). The Michigan Department of Health and Human Services (MDHHS) has blood lead level screening guidelines for children in Michigan. According to these guidelines, Medicaid requires that all children who are between 12 and 24 months of age be tested. Furthermore, children between 36 and 72 months of age who were not previously tested must also be tested at least once (MDHHS 2015). Depending on observed BLL during testing, the health department may recommend follow-up tests, provide handouts, refer families to the health department for nursing case management, and/or refer the family to the Lead Safe Home Program to determine if they are eligible for an environmental investigation and lead abatement.

Regulatory changes reduced the amount of lead in the environment leading to reductions in BLL. In 1976, the mean blood lead level in the US population was 15.8 µg/dL, while the latest biomonitoring report published in 2016 by the CDC shows a geometric mean blood lead level of 0.82 µg/dL (CDC 1982, 2019). However, it is important to note that contrary to what may be expected, significant reductions in lead exposures to the US society as a whole did not result in a corresponding increase in overall IQ measures.

Figure 2 shows BLL over time, plotted against the US National Assessment of Education Progress measures of cognitive competences for 17-year-old students. The average IQ of US high school students for 1978/1980 combined was 97.27. The average IQ increased to a peak of 99.63 in 1992, and remained fairly steady or slightly declining through 2012 (mean IQ of 98.88) (Rindermann and Pichelmann 2015). The average blood lead level in 1979 was 10 µg/dL, which represents the estimated childhood BLL that coincides with the IQ of high school students in the early 1990s. Since the mid-1970s, successful enactment of numerous federal regulations resulted in significant reductions in BLL. Nevertheless, IQ essentially remained unchanged. If lead had a significant impact on IQ at levels of 10 µg/dL or less, one would expect to see steady improvement in IQ for the nation over this same period of observation.

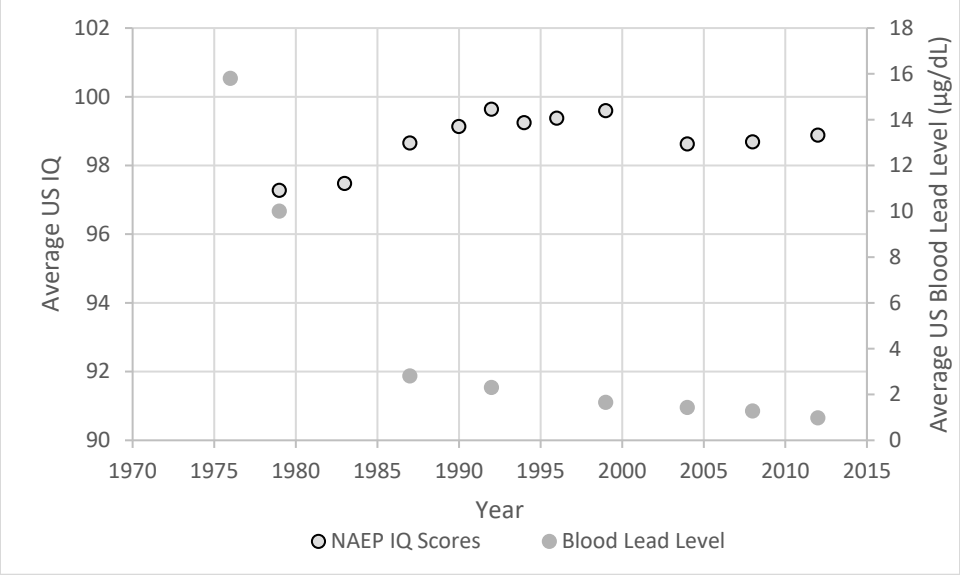

Figure 2. Changes in 17 year old IQ and reductions in blood lead levels for the US population (data extracted from CDC 1982, 2019; Dignam et al. 2019; Rindermann and Pichelmann 2015; Tsoi et al. 2016)

2.2 SEASONAL FLUCTUATIONS IN BLOOD LEAD LEVELS ARE COMMON AND NOT UNIQUE TO FLINT, MICHIGAN.

In general, consistent and predictable seasonal fluctuations in BLL have been observed in Michigan and across the United States since blood lead data became widely available in the 1970s. Fluctuations in blood lead concentrations are correlated with seasonal changes in weather patterns such as wind speed, temperature, and humidity, changes in soil moisture, and behavior of children. On average, annual peak BLL occur in mid-to-late summer, with minimums seen in the late winter months of January and February.

While seasonal fluctuations are to be expected in any population, the switch in water sources in Flint, Michigan between 2014 and 2015 resulted in many households having tap water that exceeded the maximum lead water concentrations (Gomez et al. 2018). However, as reviewed in more detail below, the change in water source occurred at approximately the same time increases in BLL would be expected based simply on the consistently observed seasonal variations.

History of Flint Water Sources and Corresponding Blood Lead Levels

From 1967 to April, 2014 the city of Flint, Michigan received its water from the Detroit Water and Sewage Departments (DWSD), known today as the Great Lakes Water Authority (GLWA), which sources its water from Lake Huron. On April 25, 2014, Flint switched sources and began using water from the Flint River that was processed through the Flint Water Treatment Plant. Recognizing the inadequacy of the new water source and treatment center, on October 16, 2015, Flint once again began receiving its water from the DWSD (Gomez et al. 2018; Kennedy et al. 2016). Several sources noted an increase in BLL among children following the 2014 switch to the Flint River water source, and they attributed the increase to that new water source (Hanna-Attisha et al. 2016; Kennedy et al. 2016). However, the observed prevalence and distribution of BLLs is dependent upon the time period of interest and sample size of children observed.

According to an analysis by Kennedy et al. (2016), at least 95% of children in Flint had a BLL within the CDC reference level (< 5 µg/dL) before, during, and after the water switch. Specifically, in order to assess the impact of the water switch, Kennedy et al. (2016) calculated the proportion of Flint children < 6 years old with elevated blood lead tests (≥ 5 µg/dL) and determined whether the odds of having an elevated BLL differed between April 2013 and March 2016. Specifically, four different time periods were evaluated: 1) before switching to the Flint River (April 25, 2013 to April 24, 2014); 2) after switching, but before the water advisory was issued (April 25, 2014 to January 2, 2015); 3) after switching, and after the water advisory was issued (January 3, 2015 to October 15, 2015); and 4) after switching back to the DWSD water system (October 16, 2014 to March 16, 2016). The proportion of children with elevated BLL during these four time periods was: 3.1% (n = 74), 5.0% (n = 84), 3.9% (n = 78), and 1.4% (n =48), respectively. Compared to BLLs before the switch, the odds of elevated BLLs immediately after the switch, but before the water advisory, was significant (aOR = 1.46; 95% CI: 1.06-2.01), after controlling for season. However, after the water advisory, late in the switch, there was no increased odds of elevated BLLs (aOR = 1.28; 95% CI: 0.92-1.76).

Gomez et al. (2018) found that the overall distribution of BLL for the population of Flint children is low with geometric mean BLL less than 1.5 µg/dL, and this was true even during the water switch. Gomez et al. (2018) analyzed BLL measured during the years of 2006 to 2016 from 15,817 Flint children aged ≤ 5 years. Specifically, during exposures to Flint River water, children's geometric mean BLL had a statistically significant increase from 1.19 µg/dL in 2014 to 1.30 µg/dL in 2015, and then a statistically significant decrease to 1.15 µg/dL in 2016. However, during the entire time period from 2006 to 2016, there was a significant decline in both the geometric mean BLL, as well as the percentage of BLL ≥ 5 µg/dL (Gomez et al. 2018).

As the water switch was not confined to a single calendar year, Gomez et al. (2019) further examined the database used in Gomez et al. (2018) to compare BLL during the 18 month period of the Flint River water change to two prior 18-month time-periods (Period I: April 25, 2006 - October 15, 2007, n = 2,095; Period II: April 25, 2012 - October 15, 2013, n = 1,834; Period III: April 25, 2014 - October 15, 2015, n = 1,734; Period III was the entirety of the water switch). The authors calculated the geometric mean (GM) of BLL in Flint children aged five years and under to account for non-normal distribution with a long upper tail. They also compared the percentage of children with elevated BLL tests (≥ 5 µg/dL) during these three periods. The geometric mean of blood lead significantly decreased from Period I to Period II to Period III (GM ± SE: 2.19 ± 0.03 µg/dL to 1.47 ± 0.02 µg/dL to 1.32 ± 0.02 µg/dL respectively, $p < 0.001$ for both decreases). The percent elevated BLL for Period I (10.6%) was statistically significantly higher than for both Period II (3.3%, $p < 0.001$) and Period III (3.9%, $p = 0.002$), but the difference between Period II and Period III was not statistically significant ($p = 0.30$).

Blood Lead Fluctuations in Flint and Nationwide

Annual blood lead concentration averages for children in Flint are available beginning in 2006, from the Hurley Medical Center, which has been the predominant source of pediatric blood lead monitoring in Flint. Between 2006 and 2016, there were 15,817 blood lead level observations available. During this time period, geometric mean BLL fell by 50.6% and the percentage of children with BLL ≥ 5 µg/dL decreased by 72.9%. However, declining trends in BLL in Flint are not monotonic, with fluctuations in BLL seen annually. While overall geometric mean BLL declined over the course of the decade, there were two years of statistically significant increases: from 1.75 µg/dL in 2010 to 1.87 µg/dL in 2011 and from 1.19 µg/dL in 2014 to 1.30 µg/dL in 2015 (**Figure 3**) (Gomez et al. 2018).

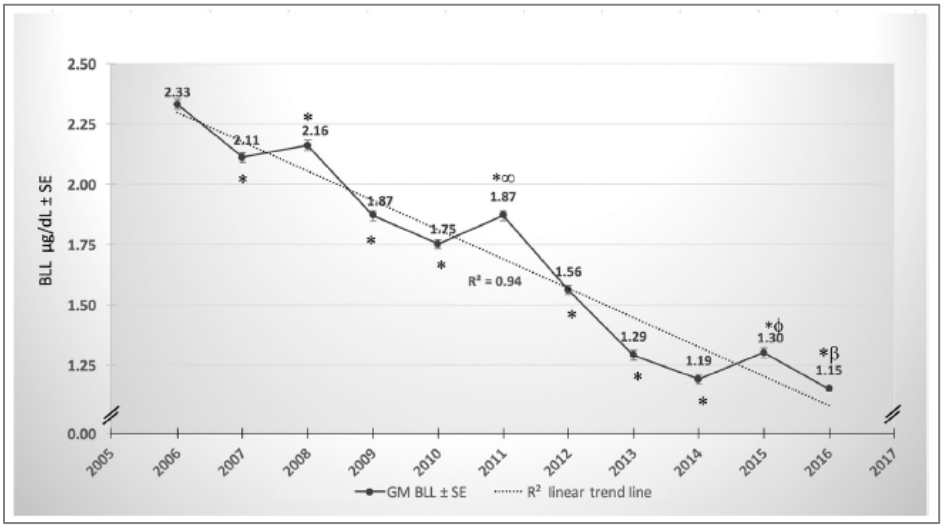

Figure 3. Trends in Flint, MI. (Gomez et al. 2018)

The Fourth National Report on Human Exposure to Environmental Chemicals was released by the CDC in 2019 (CDC 2019). This report provides summary data on numerous chemical exposures, including BLL. The current report provides summary statistics on BLL from 1999 through 2016. A review of this data shows that even on a national scale, there was an increase in measured BLL from the 2013-2014 survey cycle to the 2015-2016 survey cycle. The BLL for the 75th, 90th, and 95th percentiles of 1 to 5 year old children, increased 2.6%, 4.2% and 10.7%, respectively. This uptick occurred after years of continued decline from the 2007-2008 survey cycle through the 2013-2014 survey cycle.

Seasonal Blood Lead Level Trends throughout the United States

Beginning in 1970 and leading up to the Flint water switch in 2014, public health officials increasingly recognized the importance of blood lead monitoring in children. As screening guidelines were strengthened and surveillance programs were improved, adolescent blood lead data became widely available from local and state health departments (Ettinger et al. 2019). In 1990, only five states had comprehensive lead preventions laws, including robust surveillance systems. However, by 2010, 23 states had such programs in place (Ettinger et al. 2019; Koppaka 2011). Due to improvements in infrastructure and monitoring systems, a steady decrease in BLL was observed in children throughout the 2000s, which led to a decrease in federal funding of CDC-based lead poisoning prevention programs. Few studies are available during this period of decreased funding. However, given the refocus on BLL monitoring surrounding the Flint water switch, several studies in recent years have retrospectively examined this data. Over this 44 year period, at least one study is available to cover each decade, reporting on BLL data from a variety of locations at city, state, and national levels.

To observe seasonal BLL trends at the national level, Raymond and Brown (2015) used data collected by state and local health departments and reported to the CDC Blood Lead Surveillance. The authors reported cases of children less than five years of age with BLL exceeding 10 µg/dL by month from 2007 to 2012. The lowest number of cases were consistently reported in February and March, while the highest prevalence of cases were usually reported in July, August and September. Identical trends were observed in 2014 (Raymond and Brown 2017).

Within individual states, Haley & Talbot (2004) reported on trends in BLL of 262,687 children born in New York State between 1994 and 1997 who were screened for blood lead within two weeks of their first or second birthday. A distinct seasonal trend was observed, such that the maximum geometric mean BLL and maximum percent of children with BLL ≥ 10 µg/dL both occurred in the late summer, with minimums occurring in late winter to early spring. The percent of children with elevated BLL was 1.7 times higher in August compared to April, and the geometric mean was 1.2 times higher for the same periods. In 1998, blood lead data collection began in the state of Wisconsin for children under the age of six at their one year checkups. By 2008, data was available for a total of 676,928 children (Havlena et al. 2009). In this group, the lowest average BLL was observed in March (4.28 µg/dL), and was 15.9% lower than the highest average BLL observed in September (4.96 µg/dL). The magnitude and timing of seasonal trends was similar across the state, however, geographic stratification demonstrated the most distinct seasonal trends among those living in regions that were 80-100% urban, followed by regions that were 0-20% urban. The authors speculate the quality of housing in city centers and rural farm lands is likely to influence these trends, emphasizing exposure to lead paint and lead-containing dust.

Seasonal fluctuations in BLL are also observed in Michigan as a whole. Laidlaw et al. (2016) observed the number of cases of children with blood lead observed at levels > 5 µg/dL from the first quarter of 2010 through the fourth quarter of 2014. The highest number of elevated BLL cases were consistently observed in the third quarter (e.g. summer months) and the lowest reported number of cases was observed in the first quarter (e.g. winter months) for both the city (Flint) and the state.

Several studies noted seasonal BLL trends between 1970 and 2011 in a variety of cities across the United States. Between March of 1970 and December of 1976, Billick et al. (1979) reported trends from 178,533 quarterly BLL records in New York City children. For each year, there is defined cyclic seasonal pattern, such that the peak geometric mean blood lead level (µg/dL) is observed invariably in the third quarter (July-September) of each year (**Figure 4**). The trends persisted irrespective of race and age stratifications.

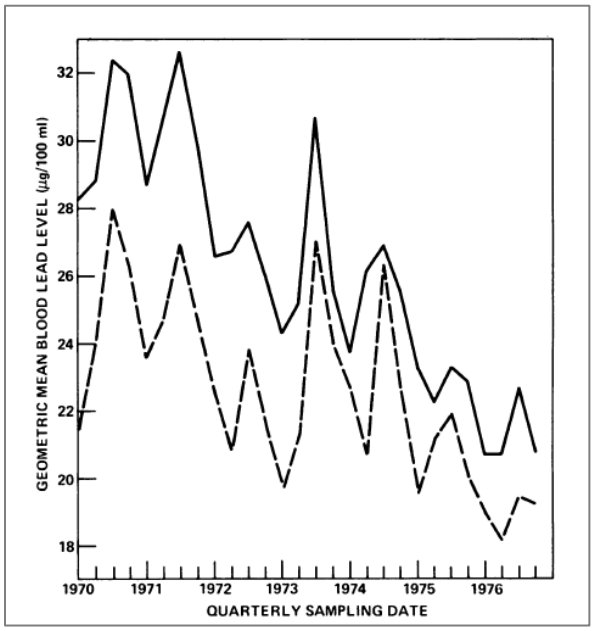

Figure 4. New York City, children 25-36 months old: (- Black) (- - Hispanic); (Billick et al. 1979)

Between April 1979 and April 1981, 250 children born in Boston, MA at Brigham and Women's Hospital provided BLL measurements up through 1983 (EPA 1995). With a maximum BLL in July of 7.52 µg/dL and minimum in February of 2.13 µg/dL, the U.S. Environmental Protection Agency concluded that there was evidence of significant seasonal variation in BLL observed in Boston over the duration of this study.

From 1986 to 1994, a seasonal trend was observed in 25,665 children between the ages of six months and seven years in Milwaukee, WI. BLL were approximately 40% higher in the summer than the winter. Using statistical models, the authors determined the maximum average BLL to occur between July and mid-September, while the minimum BLL occurred between the end of October and the beginning of March (EPA 1996).

For approximately two decades (1992-2011), 43,045 records of pediatric BLL were collected in Syracuse, NY. Shao et al. (2017) demonstrated through segmented time-series analyses that peak BLL occur in the summer, mainly June-August, and the lowest BLL occur in the winter months (Shao et al. 2017).

From 1992-1995, Yiin et al. (2000) observed a trend in BLL among 135 children aged 6-32 months in Jersey City, NJ that corresponded with both indoor and outdoor temperatures. Temperatures and blood lead concentrations (µg/dL) peaked in July and maintained minimum levels throughout the late winter in January and February, such that there was a 3.11 µg/dL difference in geometric mean BLL between the hottest and coldest months.

Similarly, from April 1, 1992 and March 31, 1993, in a smaller sample of 2,633 children under the age of five in Syracuse, NY, there was a significant 1.8 µg/dL difference in geometric mean summer BLL (GM=9.01 µg/dL, SD=1.82) compared to winter BLL (GM=7.20 µg/dL, SD=1.74; p=0.0001) (Johnson et al. 1996). In the following four years, Laidlaw et al. (2005) also noted clear

variation in BLL in Syracuse, NY from January 1994 to March 1998, with peaks most often occurring in late summer (**Figure 5**).

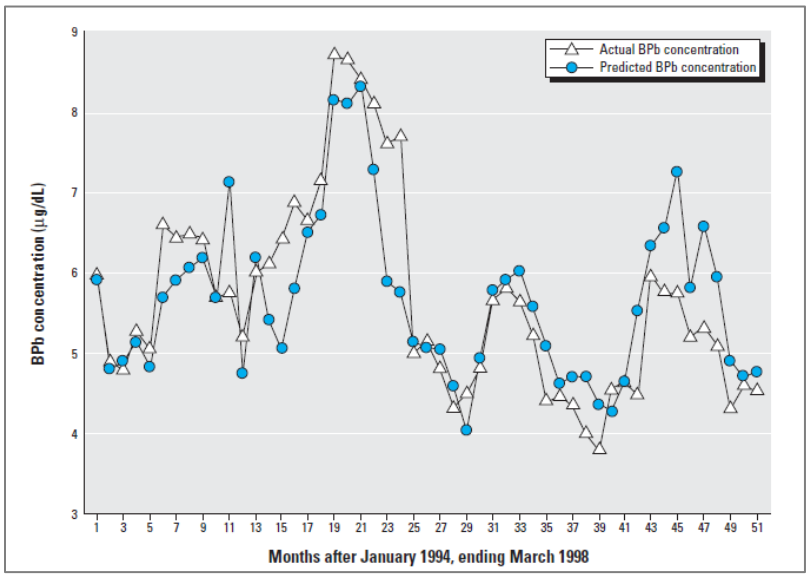

Figure 5. Syracuse, NY; (Laidlaw et al. 2005)

Explanations for Seasonal Blood Lead Level Trends

The association between blood lead concentrations and seasonal fluctuations in atmospheric lead is the most commonly reported explanation for the trend (Laidlaw et al. 2005; Laidlaw et al. 2012). Elevated concentrations of lead in soil surrounding urban areas is common due to residual effects from lead additives in gasoline, lead in exterior paint, and other industrial sources. In summer months when temperatures are high and soil moisture is low, contaminated soil particulates are likely to become aerosolized. In several cities across the rust belt of the U.S., atmospheric soil levels are between 1.27 and 1.38 standard deviations higher in June-September compared to October-May, with lead aerosol levels following the same pattern (Laidlaw et al. 2012).

Specific to seasonal trends in Flint, when Laidlaw et al. (2016) measured both blood lead and soil lead concentrations in Flint, they noted such similar patterns in time and location that they concluded, “before the change in water supply the blood peaks in the third quarters in Flint were being driven by seasonal resuspension of lead dust from contaminated soils into the atmosphere during dry periods” (Laidlaw et al. 2016, p. 9).

Several authors offered additional explanations for the season trend in BLL, stating that children play outside more often in the summer and may be directly ingesting lead in the soil (Haley and Talbot 2004; Johnson et al. 1996; Laidlaw et al. 2005). Others noted the influence of lead painted windows (Haley and Talbot 2004; Laidlaw et al. 2005). Shao et al. (2017) measured environmental lead levels and BLL before and after a paint abatement treatment, and noticed the magnitude of the seasonal trend in BLL, perhaps exacerbated by the opening and closing of lead painted windows in the summer, decreased after the abatement intervention.

Conclusions

Annual fluctuations and seasonal trends have been observed at the city, state, and national level. Such fluctuations are not new, but are directly correlated with environmental conditions, and these fluctuations have been documented since the 1970s. Peak BLL are observed in the summer months and the lowest BLL are observed in the winter. These fluctuations are observed for blood lead level measurements directly, as well as for the reported prevalence of children with BLL above a certain threshold value.

On average, children in Flint, Michigan did experience an increase in elevated blood lead values (> 5 µg/dL) in the summers of 2014 and 2015 during the Flint River water switch (Gomez et al. 2018; Kennedy et al. 2016; Laidlaw et al. 2016). However, there is significant evidence of normal fluctuations in pediatric BLL due to increases in lead in the soil and air during the warm, dry summer months. The observed increase in the BLL measured in Flint during the water source switch between April 2014 and October 2015 are not unique to Flint. The distribution of BLL for US children, as reported by the CDC, also increased during this same timeframe. The observed increase in elevated BLL in Flint during this timeframe, to a reasonable degree of scientific certainty, can be explained by increased levels of lead in indoor dust and more frequent outdoor activity, which increases exposure to lead in soil during summer months (Yiin et al. 2000).

2.3 THERE ARE KNOWN NON-CHEMICAL AND CHEMICAL FACTORS OTHER THAN LEAD THAT IMPACT INTELLECTUAL DEVELOPMENT IN CHILDREN.

The impact of the environment on intelligence is complex. There are several factors that can impact intellectual development in children. Exposures fall into two primary categories: non-chemical (e.g. quality of the home, nutrition, maternal IQ) and chemical (e.g. heavy metals, secondhand smoke). These exposures do not occur in isolation, but in a myriad of ways, which can lead to a range of effects on the cognitive development of a child.

Non-Chemical Exposures

Epidemiologists are well aware of the confounding factors and they consider a vast range of variables in their evaluations assessing the impact of lead exposures on cognition. Some confounders of interest include: the Home Observation for Measurement of the Environment (HOME) Inventory, sex, parents' level of education, maternal age at delivery, maternal IQ, socioeconomic status (SES), birth weight, birth order, feeding method (breast, bottle or both), duration of breast feeding, whether parents live together, fetal distress and growth, perinatal complications, prenatal maternal substance abuse, smoking behavior of the parents, history of anemia diagnosis, and maternal psychological status (Baghurst et al. 1992; Bellinger et al. 1992; Bradley et al. 1988; Dietrich et al. 1993; Iglesias et al. 2011; Kim et al. 2009; Tong et al. 1996; Wasserman et al. 1997). The HOME inventory is a measure of "…the quantity and quality of social, emotional, and cognitive support made available to the child in the home environment" as indicated by disciplinary methods, learning materials available to the child, amount of quality time spent with a parent, etc. (Bradley et al. 1988, p 58).

Variance is a measure of how far observed values differ from the average predicted value. Variability in cognition (e.g. IQ as measured via WISC-R), for a given lead exposure, as measured via blood lead, is high. For a given variable, the higher the variance that can be attributed to a variable, the more that outcome of interest is influenced by that variable. Numerous studies have investigated regression models to evaluate the univariate and multivariate relationship between exposure and cognition. These studies have consistently observed that non-chemical exposures

are associated with higher variance on IQ than lead exposures as measured via blood. Based on observations in the literature, the HOME inventory, SES, and parental IQ are considered the most important confounders (Koller et al. 2004). Measures of the home environment have accounted for 12% to 30% of the variance in predicted models (Baghurst et al. 1992; Iglesias et al. 2011; Wasserman et al. 1997). Socioeconomic status has been observed to account for 7% to 8.4% of the variance in IQ (Baghurst et al. 1992; Iglesias et al. 2011). One study reported that maternal IQ accounted for 19.9% of the variance and another study grouped all covariates except blood lead together and observed that they accounted for 20% of the variance (Dietrich et al. 1993; Iglesias et al. 2011). Not all studies that report the variance associated with covariates report the variance associated with BLL. Nevertheless, those that explored the contribution of blood lead level to IQ reported that it accounted for less than 1% to 6.3% of the variance (Baghurst et al. 1992; Bellinger et al. 1992; Dietrich et al. 1993; Kim et al. 2009; Tong et al. 1996; Wasserman et al. 1997). Weiss et al. (2000) evaluated the various confounding factors that are associated with cognitive deficits (e.g. pesticide exposure, other neurotoxic agents, poverty, inadequate schools, poor nutrition, teen pregnancy, poor prenatal care, maternal tobacco and drug use, low maternal education, and violent neighborhood) and noted that each factor contributes to 4% of the variance observed in IQ or roughly the equivalent of 10 µg/dL of exposure as measured via blood.

Alternative Chemical Exposures

Secondhand Smoke

There are over 7,000 chemical constituents present in cigarette smoke (DHHS 2010) and secondhand exposures are ubiquitous and hazardous to children (DiFranza et al. 2004). It is estimated that between 12 and 20% of pregnant women smoke (Makadia et al. 2017). In a systematic evaluation of smoking cessation studies of pregnant women, Schneider et al. (2010) observed that less than half of smoking women are able to fully abstain from smoking during pregnancy. Pre-natal and post-natal exposure to tobacco smoke has been shown to contribute to cognitive deficits in children (Chen et al. 2013; DiFranza et al. 2004; Makadia et al. 2017). Secondhand smoke exposure is associated with impairments in cognition and behavioral controls both of which impact school performance (Makadia et al. 2017).

One of the constituents in tobacco smoke that could possibly contribute to these outcomes is lead. Child BLL have been measured in multiple National Health and Nutrition Examination Survey (NHANES) data collection events. Cotinine levels were also captured. These studies demonstrate that children exposed to secondhand smoke in their homes have BLL that are 17% to 38% higher than children who live without smokers in the home even after adjusting for education, poverty, race, age of the home and lead dust levels in the home (Apostolou et al. 2012; Mannino et al. 2003). Nevertheless, it is important to note many studies continued to show negative associations between secondhand smoke exposure and cognitive and behavioral outcomes after adjusting for BLL. For example, Yolton et al. (2005), evaluated cognitive ability in children (6 to 16 years of age) who participated in NHANES III (n = 4399 with complete data). The researchers used serum cotinine levels in children to determine exposure to secondhand smoke. They only included children with serum cotinine levels ≤15 ng/mL, as this level had been used in prior research to discern secondhand smoke exposure. Serum cotinine levels for their included study population ranged from 0.035 to 15 ng/mL. After adjustment for poverty, parent education and marital status, sex, race, region, ferritin and blood lead level, the authors observed negative associations between serum cotinine levels and scores on reading, block design and math. This indicates that there are other constituents in secondhand smoke that contribute to the observed associations (Chen et al. 2013). At this time, there is no data to indicate a low level of secondhand exposure that could be considered harmless (DiFranza et al. 2004; Yolton et al. 2005).

Furthermore, Yolton et al. (2005) noted that observed decrements appeared to be greater at lower serum cotinine levels.

Other Chemicals in the Environment

Numerous potential environmental exposures have been shown to contribute to neurobehavioral effects. Many identified exposures are industrial chemicals shown to result in decrements in IQ of less than 10 points (Grandjean and Landrigan 2014). These changes are comparable to reported declines in IQ that show that for an increase in blood lead of 10 µg/dL, IQ has been shown to decrease by 1 to 5 points (Bellinger 2004). In a systematic review of potential environmental exposures and neurobehavioral effects, 12 chemicals that are released into the global environment were identified and included organic solvents, pesticides, and organic compounds (Grandjean and Landrigan 2014). Additional review papers have identified air pollution (nitrogen dioxide specifically), polychlorinated biphenyls (PCBs), and dioxins as exposures that are negatively associated with IQ, memory, and behavioral outcomes (Clifford et al. 2016; Liu and Lewis 2014; Zhang et al. 2017).

The strongest and most consistent associations between environmental exposure and detrimental effects on cognition are observed with exposure to air pollution. One study evaluated carbon black exposure, a marker for traffic generated particulate matter, and demonstrated deficits in composite IQ scores (-3.4; 95% CI: -6.6, -0.3), visual subscale scores (-5.4; 95% CI: -8.9, -1.9) and the general index (-3.9; 95% CI: -7.5, -0.3) of the Wide Range Assessment of Memory and Learning, after adjustment for numerous confounding factors including exposure to secondhand smoke and peak blood lead level (Suglia et al. 2008).

Two reviews on the cognitive effects of air pollution (Clifford et al. 2016; Sram et al. 2017) strongly supported the relationship between pre- and post-natal exposure to particulate matter (PM) and polycyclic aromatic hydrocarbons (PAH) and adverse mental and behavioral outcomes in adolescents. PM and PAH are persistent pollutants, and increased levels are common to urban areas due to combustion sources such as coal burning, and traffic related emissions from diesel- and gasoline-powered vehicles. Health studies primarily focus on two categories of PM, classified by particle size – PM_{10} and $PM_{2.5}$. PM_{10} are particles with diameters of 10 micrometers or smaller, and $PM_{2.5}$ are particles with diameters of 2.5 micrometers or smaller. Both particulate classifications are small enough to be inhalable, and thus, pose a health risk.

A longitudinal cohort study of mother-child pairs was used to evaluate maternal prenatal exposures to air pollution on neurodevelopment outcomes in early childhood. Subjects participated in the Mothers and Children's Environmental Health Study and outcomes were assessed at 6, 12 and 24 months. Statistically significant negative associations were observed for prenatal exposure to PM_{10} and two outcomes: the mental development index (MDI) ($\beta = -2.83$; $p = 0.003$) and the performance development index (PDI) (PM_{10}: $\beta = -3.00$; $p = 0.002$), after adjusting for covariates (Kim et al. 2014). During pregnancy, an increase of 4.40-8.7 µg/m^3 in $PM_{2.5}$ exposure led to increased odds of autism spectrum disorder (ASD) ranging from about 7% to 108% in three U.S. based studies (Becerra et al. 2013; Raz et al. 2015; Volk et al. 2013). Additionally, among adolescent-aged children in Barcelona (n=2,618 children, mean age=8.5 yrs.), a study of traffic-related $PM_{2.5}$ in 39 schools demonstrated that a 3.8 µg/m^3 increase in $PM_{2.5}$ was associated with significant decreases in working memory (-5.6; 95% CI: -10.7, -0.5) and superior working memory (-5.1; 95% CI: -9.2, -1.1) (Basagana et al. 2016). The significant findings from all studies persisted even after controlling for relevant maternal and paternal sociodemographic status and birth outcomes.

Perera et al. published several papers (2006; 2009) on the impact of several environmental exposures, including PAHs, on cognitive development in a prospective cohort of children born to African-American and Dominican mothers in New York City. In 2006, Perera reported that high prenatal exposure to PAHs (≥ 4.16 ng/m^3) was associated with lower mental development index at age three (-5.69; 95% CI: –9.05, –2.33; p < 0.01) and the odds of cognitive developmental delay were also significantly greater for children with high prenatal exposure (OR =2.89; 95% CI: 1.33, 6.25; p = 0.01). Two years later, at age five, children in the same cohort with PAH levels above the median of 2.26 ng/m^3 demonstrated full-scale (p=0.007) and verbal (p=0.003) IQ scores that were 4.31 and 4.67 less than children with PAH levels below the median, respectively. Similar effects of environmental pollutants, such as PAHs, were observed among children in Poland (n=170). The relative risk of depressed verbal IQ (Dep VIQ; measured as the difference between Wechsler Intelligence Scale for Children-Revised and verbal IQ) increased threefold for each log unit increase in cord blood PAH adducts (95% CI: 1.3, 6.7). Post-natal PAH exposure was also significantly related to Dep VIQ (RR=1.6; 95% CI: 1.1-2.5) (Jedrychowski et al. 2015). In the same cohort, Edwards et al. (2010) observed a negative relationship between PAH exposure above 17.96 ng/m^3 and nonverbal reasoning ability (measured with Raven Colored Progressive Matrices) that persisted after adjustment for several covariates, including lead exposure.

Conclusions

Many factors contribute to cognitive and behavioral outcomes in children. The literature consistently demonstrates that non-chemical exposures (measures of the home environment) account for the highest variance observed in predictive models and BLL account for the least. With regard to chemical exposures, there are common alternative exposures that have also been linked with decrements in cognitive and behavioral outcomes. One common chemical exposure found within the home is secondhand exposure to combustible cigarette smoke. There are thousands of chemicals in tobacco smoke, and current research shows that there is no minimal level of exposure to secondhand smoke that is considered safe for children.

In addition to exposures within the home environment, environmental exposure to air pollution is associated with declines in cognitive and behavioral performance. Particulate matter and PAH exposure are associated with declines in IQ that are equivalent to those estimated due to low lead exposures. Many of these associations remain, even after adjusting for lead exposure.

2.4 Based on the Scientific Evidence to Date, Blood Lead Levels Less than 5 µg/dL are Not Causally Associated with Decrements in Cognitive Abilities in Children.

Government Perspective on Blood Lead Levels

Centers for Disease Control and Prevention

In 2012, the CDC Advisory Committee on Childhood Lead Poisoning Prevention (ACCLPP) recommended the elimination of the term “blood lead level of concern.” This was due to published literature demonstrating negative associations between BLL less than 10 µg/dL and academic achievement and behavioral domains like attention deficit hyperactivity disorder (ADHD) (ACCLPP 2012). In replacing the old terminology, CDC recommended designating a reference value of elevated BLL based on the 97.5th percentile of NHANES generated distribution of BLL for 1 to 5-year-old children. This current level is 5 µg/dL and is based on the distribution of BLL

collected from 2007 to 2010 (Caldwell et al. 2017). A history of the blood lead level intervention levels is shown in Table 1.

Table 1. Historical designation of intervention levels of measured childhood blood lead levels (ACCLPP 2012; Lanphear et al. 2005; NTP 2012a)

Year	Intervention Level (µg/dL)
1960	60
1971	40
1978	30
1985	25
1991	15
2005	< 10
2012	5

In their 2012 report, ACCLPP emphasized primary prevention and stated that "[i]n the U.S., this strategy will largely require that children not live in older housing with lead-based paint hazards" (p. ix). The ACCLPP noted that additional research was needed to develop interventions to maintain BLL < 5 µg/dL for those residing in pre-1978 housing.

National Toxicology Program

The National Toxicology Program (NTP) of the US Department of Health and Human Services authored a monography on the "Health Effects of Low-Level Lead." The purpose of the monograph was to evaluate the evidence published to date regarding the health effects associated with low-level lead exposure. Low-level lead was defined as a blood lead level < 10 µg/dL. According to the NTP, there is sufficient evidence for adverse health effects in children and adults at BLL < 10 µg/dL. Further they noted that there was sufficient evidence that BLL < 5 µg/dL in children are associated with lower academic achievement, decreased IQ, and reductions in specific cognitive measures.

Informative Literature

The CDC ACCLPP and the NTP reviewed numerous studies, but indicated that there were key papers that drove their conclusions of significant associations between BLL < 5 µg/dL and deficits in cognitive and behavioral outcomes in children. Canfield et al. (2003) measured associations between IQ and blood lead level in children (n = 172) residing in Boston; Bellinger and Needleman (2003) re-analyzed data from a subset of the Boston cohort (n = 48) whose blood lead level never exceeded 10 µg/dL; and Lanphear et al. (2005) conducted a pooled analysis of several prospective cohort studies (ACCLPP 2012).

Canfield et al. (2003) evaluated associations between lead exposure and children's performance in IQ tests with a focus on children whose blood lead concentrations never exceeded 10 µg/dL. Venous blood lead samples were collected at 6, 12, 18, 24, 36, 48, and 60 months of age. The Stanford-Binet Intelligence Scale, 4th edition was given to each child (n = 172) at the ages of 3 and 5 years. The composite score of results from the vocabulary, spatial pattern analysis, quantitative ability, and memory was used because it is most similar to other tests of intelligence. Confounders included the child's sex, birthweight and iron status; and the mother's IQ, years of education, race, tobacco use during pregnancy, yearly household income, and the HOME score.

86 children had peak blood lead concentrations < 10 µg/dL. Overall BLL were provided for the entire sample (peak blood lead level of 11.1 µg/dL for children with complete data), but no overall estimate was provided for children in the subset of interest. Data on the number of children with BLL below 5 µg/dL were also not reported. Linear regression analyses showed that for a 1 µg/dL increase in average blood lead concentration, IQ declined 1.37 (95% CI: -2.56, -0.17) points. Non-linear mixed models observed that for an increase in blood lead from 1 µg/dL to 10 µg/dL, IQ was predicted to decline 7.4 points.

Upon learning of these findings, Bellinger and Needleman (2003) presented a subset analysis of a prospective cohort of children living in Boston (n = 48). In this updated analysis, the authors observed that the coefficient for blood lead level for those subjects who never exceeded 10 µg/dL was greater (-1.56) than the blood lead coefficient for the entire sample population (-0.58), p = 0.03. In the original study, the children (n=148) had BLL that ranged from 0 to 25 µg/dL at 24 months (Bellinger et al. 1992). Approximately 10% of the children had BLL of 3 µg/dL or less and the mean blood lead level was 6.5 µg/dL at 24 months. BLL were assessed at 6, 12, 18, 24, and 57 months. The Wechsler Intelligence Scale for Children-Revised (WISC-R) and Battery Composite scores on the Kaufman Test of Educational Achievement – Brief Form (K-Tea). The mean age of the children during the neuropsychological assessments was 9 years 9 months. For the regression analyses, the following confounders were included: medical and educational history of the child, family structure and sociodemographic characteristics, Family Adaptability and Cohesion Evaluation Scales, Social Readjustment Rating Scale, Parenting Stress Index, Children's Life Events Inventory-Revised (modified), and Social Support Network, HOME score, maternal IQ, and birth weight. After adjustment, an increase in 10 µg/dL at 24 months was associated in a decrease in IQ of 5.8 points (95% CI: 1.7, 9.9). BLL at 24 months only accounted for 3.2% of the variance in the full-scale IQ scores.

A pooled analysis of seven prospective cohort studies, including the two studies above, assessed BLL and IQ (Lanphear et al. 2005). All studies were initiated before 1995 and included the following locations: Yugoslavia; Australia; Rochester, NY; Cincinnati and Cleveland, OH; Boston, MA; and Mexico City, Mexico. Intelligence tests were administered at 10 years of age for the Boston cohort, and between 4 years 10 months and 7 years of age for the remaining cohorts. Blood samples were collected at 6, 12 (or 15), 36, 48, and 60 months of age. A total of 1,333 children had data on IQ, blood lead, and covariates of interest: maternal IQ, HOME score, birth weight, and maternal education. The median peak blood lead concentration was 18 µg/dL and the lifetime average blood lead level was 12.4 µg/dL. Only 18% and 8% of the children had maximum BLL < 10 µg/dL and < 7.5 µg/dL, respectively. No data was provided on the number of children with maximum BLL < 5 µg/dL. The authors observed intellectual deficits among children whose maximal BLL never exceeded 7.5 µg/dL and further stated that the larger sample size from the pooled analysis showed that there was a significantly greater reduction in those exposed at levels < 7.5 µg/dL than those exposed to ≥ 7.5 µg/dL. It was also noted that average lifetime estimates of lead exposure and concurrent BLL were stronger predictors of intellectual deficits than peak BLL. No evidence of a threshold level of exposure was observed in this pooled analysis.

Observations and Re-analysis of the Lanphear et al. (2005) Pooled Prospective Cohort Analysis

Potential Exposure Misclassification

According to Lanphear et al. (2005), "[t]he objective of this study was to examine the association of intelligence test scores and blood lead concentration, especially for children who had maximal measured BLL < 10 µg/dL" (p. 894). There are some discrepancies between the pooled studies

as cited by Lanphear et al. (2005) and as cited by the original study authors (Baghurst et al. 1992; Bellinger et al. 1992; Canfield et al. 2003; Dietrich et al. 1993; Ernhart et al. 1989; Schnaas et al. 2000; Wasserman et al. 1997). Most of these inconsistencies can be explained by the different exclusion criteria used in the pooled analysis. However, there are some remaining disagreements in exposure classification that remain unexplained, especially with regards to peak exposures. Lanphear et al. (2005) defines peak BLL as the maximum value measured prior to an IQ test and states that these IQ tests were conducted when the children were between 4.8 years and 10 years of age, depending on the cohort. Furthermore, Lanphear et al. (2005) states that the mean age for peak BLL occurred at 2.5 years of age.

It is imperative that exposures for these children are known and well characterized because of the exposure-response relationship under investigation. Table 2 of the Lanphear et al. (2005) study states that there were 23 children in the Cincinnati cohort and 103 children in the Rochester cohort with peak blood lead < 10 µg/dL. However, these counts do not align with the numbers reported in the original reports of the populations in Dietrich et al. (1993) and Canfield et al. (2003), respectively. On page 39 of the Dietrich et al. (1993) manuscript, the authors state that "[v]irtually all of the children (95%) exceeded 10 µg/dL in the first five years of life." It follows then, that only 5% (i.e., 12 or 13) of the 253 children from the original cohort had peak blood lead below 10 µg/dL, which is just over half of what was reported in Lanphear et al. (2005). Furthermore, Lanphear is co-author on publications reporting on longitudinal evaluations of the Cincinnati cohort where it is reported that of the original cohort sample (n = 305), 99% of this cohort had peak BLL above 10 µg/dL (Cecil et al. 2008; Cecil et al. 2011). That would mean that only three children in the Cincinnati cohort had peak BLL < 10 µg/dL. This means that depending on citation, between 10 and 20 children from the Cincinnati cohort were classified incorrectly. On page 1520 of the Canfield et al. (2003) manuscript, the authors report that "71 of these children had [a peak blood lead concentration below 10 µg/dL] at both [3 and 5 years of age.]" This means 32 children from Rochester were classified incorrectly. Taken together, approximately 42 to 52 of the 244 (17.2% to 21.4%) children reported to have BLL below 10 µg/dL may have been misclassified. In other words, 200 children or fewer are being used to extrapolate a curve and define an association between BLL less than 10 µg/dL and IQ decrements. As described below, even if the data is taken at face value as indicated by Lanphear et al. (2005), there is very little statistical power to reach definitive conclusions for peak BLL < 7.5 µg/dL and current BLL < 5 µg/dL (Crump et al. 2013).

These observations are separate and distinct from those described below regarding the Crump et al. (2013) re-analysis of the Lanphear et al. (2005) pooled analysis. However, it is important to note the Crump et al. (2013) used a database of the pooled studies that increased the overall sample size to 1493 but the total number of children (n = 88) with peak BLL < 7.5 was lower than reported by Lanphear et al. (2005; 2019).

Crump et al. (2013) Re-Analysis

Crump et al. (2013) performed a re-analysis of the pooled prospective cohort study conducted by Lanphear et al. (2005). There were three key differences in the update analysis: non-lead explanatory variables were defined in a site-specific manner, which permitted control of more variables than the original analysis, summary blood lead variables were defined using more of the available data, and different transformations in BLL were used in the modeling evaluating associations between exposure and IQ. Crump et al. (2013) also noticed that in the original assessment the Boston cohort IQ, tests were not concurrent with ascertainment of BLL. For the updated analysis, Crump and colleagues used IQ tests and BLL ascertained at 57 months. Similarly, the data for the Cincinnati cohort was updated to ensure the use of concurrent evaluations of IQ and BLL. The updated assessment also considered additional confounders than

those used by Lanphear et al. (2005). A stepwise procedure was used to ensure all variables in the model were significant at a p-value ≤ 0.15, resulting in adjustment for site, HOME score, maternal education, maternal IQ, birth weight, maternal alcohol use, maternal smoking habit, and birth order.

Other observations, which could influence evaluations of associations between low-level lead exposure and IQ, were noted. Lanphear et al. (2005) performed log transformations of blood lead variables. This transformation can lead to inflated estimated IQ because as BLL approach zero, predicted IQ scores approach infinity. There were members of the Boston cohort with BLL reported as 0 µg/dL for which they were assigned an arbitrary value of 0.1 µg/dL. Crump et al. observed that the Lanphear analysis was sensitive to these very low BLL and "[t]his sensitivity underscores the fact that [log transformed blood lead] is not a good transform for studying low exposure effects" (Crump et al. 2013, p. 789).

The transformation employed by Crump et al. (2013) was the natural log of the sum of measured blood lead plus the value of 1. This approach resulted in a model that was not sensitive to low BLL. Crump et al. did observe that the non-linear model is a better predictor of IQ than the linear blood lead model over the full range of blood lead data. Nevertheless, it was observed that for BLL ≤ 10 µg/dL a linear model is appropriate and describes the exposure-response of low-lead exposures. The authors were able to estimate decrements in IQ for peak BLL of at least 7 µg/dL (-3.52; 95%CI: -6.60, -0.44). However, due to low sample size, the confidence limits become so wide at levels of 6 µg/dL or less that almost no information is provided. As part of a sensitivity analysis, 5% of the most influential points were removed and the authors noted associations between IQ and BLL as low as 6 µg/dL. In the updated analysis "only concurrent [blood lead] showed a significant [blood lead] association with IQ for peak [blood lead] values < 7.5 µg/dL, and no [blood lead] showed a significant association for peak [blood lead], 10 µg/dL" (Crump et al. 2013, p.797).

The authors could not challenge the Lanphear et al. (2005) conclusion of no threshold level of lead exposure and effects on IQ. Based on available data, "concurrent [blood lead] provided evidence for an association of [blood lead] with IQ at peak [blood lead] exposure below 7 µg/dL (and possibly as low as concurrent [blood lead] of 5 µg/dL in our analysis)" (Crump et al. 2013, p. 798).

Additional Prospective Cohort Analyses

In order to properly ascertain the relationship between BLL in a given population and its associated effect on cognition and neurological development, data drawn from the literature must be in accordance with the distribution of blood lead seen in the population of interest—in this case, Flint, Michigan. As discussed previously, Gomez et al. (2018) found that children's geometric mean BLL significantly increased from 1.19 µg/dL in 2014 to 1.30 µg/dL in 2015, and then significantly decreased to 1.15 µg/dL in 2016. Gomez et al. (2019) further examined the geometric mean BLL and percentages of BLL ≥5 µg/dL in three periods: Period I: April 26, 2006-October 15, 2007 (earliest timeframe available the study) and Period II: April 25, 2012-October 15, 2013 (timeframe immediately before the switch), were compared to Period III: April 25, 2014-October 15, 2015 (Flint River water exposure). The BLL (geometric mean ± standard deviation) significantly decreased from Period I to Period II (2.19±0.03 µg/dL to 1.47±0.02 µg/dL, respectively; $p < 0.001$) and from Period I to Period III (1.32±0.02 µg/dL; $p < 0.001$). Moreover, the percentage of BLL ≥5 µg/dL significantly decreased from Period I to Period II (10.6% to 3.3%, respectively; $p < 0.001$) and from Period I to Period III (3.9%; $p = 0.002$) (Gomez et al. 2019).

As previously discussed, Lanphear et al. (2005) conducted a pooled analysis of seven prospective cohort studies that assessed BLL and IQ and subsequently, in 2019, published an erratum of their 2005 study (Lanphear et al. 2019). Notably, the BLL in both the original and updated analyses were higher than the aforementioned measurements in Flint children, even during the timeframe of potential exposure to Flint River water. As described above, 5% or fewer children in Flint had elevated BLL during the switch. Over 90% of the children in the pooled analysis had BLL above 7.5 µg/dL. Furthermore, Lanphear et al. (2019) reported that the median peak blood lead concentration was 18 µg/dL and the lifetime average blood lead level was 11.9 µg/dL.

The original pooled analysis was published 15 years ago. Lanphear et al. (2005) made some corrections, when they published the updated analysis. However, the authors continued to use blood lead tests that were not concurrent with IQ tests for some cohorts. This is important to note because IQ test scores have been shown to change throughout childhood (Moffitt et al. 1993). The observed association could be biased due to the time difference between the blood lead and cognitive tests. Finally, the sample size of children with BLL < 7.5 µg/dL was small. No efforts were made to include additional longitudinal studies in the updated analyses even though a number of published studies have been published in the interim.

Between the original analysis (Lanphear et al. 2005) and the corrected analysis (Lanphear et al. 2019), ATSDR identified seven new prospective studies that evaluated the associations between BLL and FSIQ in children were published (ATSDR 2020). The updated studies cited by ATSDR were conducted in Cleveland, OH (Min et al. 2009), Mexico City, Mexico (Braun et al. 2012; Kordas et al. 2011; Schnaas et al. 2006), Rochester, NY (Jusko et al. 2008), Canada (Desrochers-Couture et al. 2018), and in the United Kingdom (Taylor et al. 2017). Of these studies, six (Schnaas et al. 2006; Min et al. 2009; Kordas et al. 2011; Braun et al. 2012; Taylor et al. 2017; Desrochers-Couture et al. 2018) would have potentially met the inclusion criteria for the Lanphear et al. (2005, 2019) analyses, while one of the studies (Jusko et al. 2008) would not have. Notably, Jusko et al. (2008) was a follow-up of an existing cohort previously published by Schnaas et al. (2006), which was included in the analyses by Lanphear et al. (2005, 2019). The six recent prospective cohort studies that have been published since Lanphear et al. (2005) provide the opportunity to update the original analysis. When qualitatively compared, the distribution of BLL among Flint children were lower than the blood lead distribution of children in most of the recently published prospective cohort studies.

Schnaas et al. (2006)

Schnaas et al. (2006) evaluated a cohort of children who had geometric mean BLLs ≥ 5 µg/dL at various pre- and post-natal points. Specifically, Schnaas et al. (2006) conducted a prospective cohort study among children born in Mexico City, Mexico, between 1987 and 1992 to examine the association between prenatal and postnatal lead exposure with intellectual development. Of 321 infants who met the inclusion criteria and were originally enrolled in the study, 175 were tested after five years of age, and only 150 had complete data and were included in the analyses. Prenatal BLL were measured at 12, 20, 28, and 36 weeks of pregnancy, cord BLL were measured at delivery, and child's BLL were measured from birth to age five every six months, and then annually from ages 6 to 10 years. The Wechsler Intelligence Scale for Children – Revised (WISC-R) was used to measure child intelligence from six to 10 years of age. The pattern of blood lead level effects on FSIQ from six to 10 years of age was analyzed using linear mixed models with random intercept and slope. The geometric mean BLL during pregnancy, from 1-5 years, and from 6-10 years, respectively, were 8.0 µg/dL (range = 1-33), 9.8 µg/dL (range = 2.8-36.4), and 6.2 µg/dL (range = 2.2-18.6). Specifically, geometric mean BLL were ≥10 µg/dL from ages 1 to 4 years, including 10.8 µg/dL at age one, 12.8 µg/dL at age 2, 11.3 µg/dL at age 3, and 10.3 µg/dL

at age 4. BLL subsequently continued decreasing from 9.3 µg/dL at age 5, 7.9 µg/dL at age 6, 7.5 µg/dL at age 7, 6.4 µg/dL at age 8, 6.0 µg/dL at age 9, to 5.6 µg/dL at age 10. In fixed-effect longitudinal regression analyses adjusted by maternal IQ, socioeconomic status, sex, birth weight, and age of first FSIQ test, the only childhood BLL that was statistically significantly associated with FSIQ score was the mean of annual BLL measures from 6 to 10 years old (β = -2.54; 95% CI: -4.09, -0.81; p = 0.003). However, the linear mixed model with random intercept and slope did not result in statistically significant findings for any childhood BLL. It is important to note that the child BLL from ages 1 to 10 are higher than the BLL of Flint children, and therefore, the results of this study have limited applicability to Flint.

Min et al. (2009)

In a prospective cohort study of urban children, Min et al. (2009) evaluated the association between childhood lead exposure measured at 4 years of age and children's IQ and academic achievement measured at 4, 9, and 11 years of age. A total of 278 inner-city children (86% African American; 98% low SES; and 88% prenatally exposed to at least one substance, including cigarettes, cocaine, marijuana, and/or alcohol) from Cleveland, OH who were recruited at birth between September 1994 and June 1996.

BLL were not measured until age four, at which time the mean blood lead level was 7.01 µg/dL (SD = 4.07; range = 1.3-23.8). Specifically, at age 4, 36% (n = 100) of children had BLL < 5 µg/dL, 26% (n = 71) had BLL between 5 and 7.5 µg/dL, 20% (n = 55) had BLL between 7.5 and 10 µg/dL, and 19% (n = 52) had BLL ≥10 µg/dL. Full Scale, Verbal, and Performance IQ were measured using an abbreviated Wechsler Preschool and Primary Scales of Intelligence-Revised that was administered to children at 4 years of age. Subsequently, the Wechsler Intelligence Scales for Children – Fourth Edition and the Woodcock Johnson-III Tests of Achievement was administered to children at both 9 and 11 years of age to evaluate Full Scale IQ, verbal comprehension, perceptual reasoning, working memory, processing speed, math, and reading scores (Min et al. 2009).

The study authors found that with each 10 µg/dL increase in blood lead level at age 4, there was an estimated 4.1 to 5.4 Full Scale IQ point loss at ages 4, 9, and 11 ($p<0.05$). Additionally, BLL at age 4 were significantly associated with decrements in Performance IQ at age 4 (β = -0.74, $p<0.001$), perceptual reasoning at age 9 (β = -0.45, $p<0.05$) and age 11 (β = -0.61, $p<0.01$), reading scores at age 9 (β = -0.58, $p<0.05$) and age 11 (β = -0.60, $p<0.01$), and verbal comprehension (β = -0.51, $p<0.01$) and math scores at age 11 (β = -0.45, $p<0.05$). Among a subgroup of children with BLLs <10 µg/dL, analyses demonstrated that children with BLL from 5 to <10 µg/dL (compared to children with BLLs < 5 µg/dL), had significantly worse Performance IQ at age 4 (p = 0.01), perceptual reasoning at age 9 (p = 0.01), and reading scores at age 9 (p = 0.003) and age 11 (p = 0.04) (Min et al. 2009).

While the authors concluded that early low level, lead exposure effects cognitive outcomes and school achievement through late childhood, this conclusion has limited application to the children of Flint. The BLL for children in this study were not evaluated until age 4 years and therefore would not have accounted for children who had BLLs > 10 µg/dL earlier or later in life. Generally, peak BLL in children are usually observed around two years of age, and it is likely that peak blood lead level for these children was higher than those observed at the time of testing (Hornung et al. 2009).

Kordas et al. (2011)

Kordas et al. (2011) aimed to determine if polymorphisms in two genes that mediate dopaminergic neurotransmission (i.e., DAT1 and DRD2) modify the relationship between pre- or post-natal lead exposure (via cord blood, and 24- and 48-month blood lead measures) and neurocognitive development. These analyses examined mother-infant pairs who received prenatal care between January 1994 and June 1995 at three hospitals that serve low-to-middle income populations in Mexico City, Mexico.

Of the 617 infants who qualified for the study, 220 had complete data at the 24-month visit, and 186 had complete 48-month visit. Neurocognitive outcomes at 24-months were measured with the mental development index (MDI) and psychomotor development index (PDI) of the Bayley Scales of Infant Development II (BSID-II), and at 48-months, cognition was measured with the General Cognitive Index (GCI) and memory scale of the McCarthy Scales of Children's Abilities. In this sample, the arithmetic mean umbilical cord blood lead concentration was 6.6 (SD=3.3) µg/dL with 13.6% of samples with concentrations at or above 10 µg/dL. The mean BLL at 24- and 48- months were both 8.1 (24-month SD=4.4, 48-month SD=3.6) µg/dL, and 23.2% and 21.0% of children had blood lead concentrations at or above 10 µg/dL, respectively (Kordas et al. 2011).

Ultimately, there were no statistically significant interactions between DAT1 or DRD2 and cognitive performance measures or blood lead exposure, and therefore, the authors concluded that DAT1 and DRD2 do not modify the association between pre- or post-natal lead exposure and neurocognitive outcomes. Nevertheless, blood lead concentrations were independently associated with developmental scores. Namely, each 1 µg/dL of cord blood lead was associated with 0.7-point (SE=0.3) lower 24-month MDI scores ($p<0.05$), and each 1 µg/dL of concurrently measured blood lead at 48 months was associated with a 0.6-point (SE=0.2) lower GCI score ($p<0.05$), and a 0.3-point (SD=0.1) lower memory score ($p<0.01$). All models were adjusted for birth weight, gestational age, sex of child, maternal characteristics (age, years of schooling, IQ, ever smoker, and marital status at enrollment), and household characteristics (crowding and type of floor in home). However, the association was not consistent across all time points, as there was no statistically significant associations between 24-month BLL and concurrently measured MDI or PDI scores, nor between cord blood lead and the PDI, GCI, or memory scores (Kordas et al. 2011).

The BLL in this cohort are higher than those of children in Flint, MI.

Braun et al. (2012)

Braun et al. (2012) assessed whether blood lead concentrations at different times during early childhood were more strongly associated with deficits in cognitive abilities at age 4. Data for this study come from 1,035 mother-child pairs from low to moderate-income households who participated in four prospective birth cohorts between 1993 and 2006 in Mexico City, Mexico. Women were excluded if they planned to leave the area within five years, had a history of conditions (i.e., infertility, diabetes, or psychosis), consumed alcoholic beverages daily during pregnancy, were addicted to illegal drugs, were diagnosed as a high-risk pregnancy, or were pregnant with multiples. Blood lead was measured longitudinally between 1997 and 2007 in children at ages 1, 2, 3, and 4 years, while child cognitive abilities were evaluated using the general cognitive index (GCI) of the McCarthy Scales of Children's Abilities at 4 years of age. Notably, the average blood lead concentration among children with complete follow-up at age four was higher than those with missing data (geometric mean of 5.3 µg/dL versus 4.9 µg/dL; percent difference = 7%, 95% CI: 0 to 13%). Among children with complete follow-up data, median blood lead concentrations were 4.2 µg/dL (range = 0.3-27.4), 4.6 µg/dL (range = 0.6-36.8), 5.5 µg/dL

(range = 0.6-50.1), and 5.9 µg/dL (range = 0.3-30.3), respectively, at 1, 2, 3, and 4 years of age. The blood lead concentrations at 2 years were most strongly associated with reduced GCI scores at 4 years, such that each 10 µg/dL increase in blood lead concentrations was associated with a 3.8 point (95% CI: –6.3 to –1.4) decrease in GCI scores. The authors concluded higher blood lead concentrations among children 2 years of age were most predictive of decreased cognitive abilities in this cohort, after adjusting for confounders.

The BLL in this cohort are higher than those of children in Flint, MI.

Taylor et al. (2017)

Taylor et al. (2017) examined prenatal and 30-month postnatal blood lead measurements and child IQ scores from mother-infant pairs in the population-based Avon Longitudinal Study of Parents and Children (ALSPAC). In this England-based study, the authors aimed to determine if there were sex differences in the influence of lead exposure on IQ, and to determine the moderation effect of prenatal lead exposure on child IQ.

Among the 4,316 live births, 348 children had complete data at the age four measurement, and 1,826 (1,823 for total IQ only) had complete data at the age eight measurement. The arithmetic mean prenatal blood lead concentration was 3.67 (SD = 1.46) µg/dL, and the mean 30-month blood lead level was 4.22 (SD = 3.12) µg/dL, resulting in 14.3% of mothers and 26.6% of children with BLL greater than 5.0 µg/dL. IQ at age four was measured with Wechsler Pre-school and Primary Scale of Intelligence – Revised UK edition (WPPSI), and IQ at age eight was measured with the Wechsler Intelligence Scale for Children (WISC-III) (Taylor et al. 2017).

The results of these analyses showed no association between prenatal lead exposure with child IQ at 4 or 8 years old when adjusting for numerous demographic, social, and maternal behavioral variables, and no moderation of the association between child blood lead and IQ. Interestingly, in girls only, there was a significant positive association between verbal IQ and total IQ at age 8, such that each 1 µg/dL increase prenatal blood lead concentration was associated with a 0.71 points higher verbal IQ score (95% CI: 0.11 to 1.32; p=0.021) and a 0.73 points higher total IQ score (95% CI: 0.13-1.33; p=0.017). Conversely, the coefficients tended to be negative in boys (-0.15, -0.42, and -0.29 points, respectively), although none of the associations were statistically significant.

There were no significant, negative associations between lead and IQ scores in any analysis. Overall, the cohort of this study has the most comparable exposure levels to the children of Flint, and this study demonstrated that these levels are not associated with decrements in IQ.

Desrouchers-Couture et al. (2018)

Finally, a recent study by Desrouchers-Couture et al. (2018) evaluated the associations between various blood lead measures (e.g., maternal blood lead, cord blood lead, and childhood blood lead) and cognitive function in Canadian preschoolers. Specifically, data were obtained from 609 mother-child pairs who were mostly middle to upper class families from the Maternal-Infant Research on Environmental Chemicals (MIREC) Study.

Lead was measured in maternal blood, cord blood, and in children between the ages of three and four. The Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III) was administered to children at ages 3 to 4 years to measure their cognitive function, concurrently with the childhood blood lead. The association between WPPSI-III scores and BLL were evaluated using multiple linear regression, adding child sex as a moderator. The geometric mean for lead levels in maternal blood during the first and third trimesters, in cord blood, and in child blood, respectively, were 0.62

µg/dL (SD = 1.6; range = 0.16-4.14), 0.59 µg/dL (SD = 1.7; range = 0.14-3.93), 0.76 µg/dL (SD = 1.7; range = 0.08-3.52), and 0.70 µg/dL (SD = 1.7; range = 0.14-5.49) (Desrochers-Couture et al. 2018).

There were no significant differences between boys and girls for any of the measured blood lead concentrations. Using confounder-adjusted multiple regression models, the authors found no significant associations between maternal blood lead, cord blood lead, or childhood blood lead concentrations and WPPSI-III scores. Further analyses were conducted to assess potential difference by sex in the association between cord and childhood lead concentrations with IQ scores, which demonstrated a significant modification by sex of the association between cord blood lead concentrations and Performance IQ scores.

Specifically, there was a significant inverse relationship between cord blood concentrations and Performance IQ in boys (β = -3.28; SE = 1.62; 95% CI: -5.31, -1.18; p = 0.01), while this relationship was not observed among girls. The BLL in this cohort were similar to Flint children, and overall results did not demonstrate an association with IQ and concurrent or maternal BLL, although an inverse association was observed only for boys' cord BLL and Performance IQ.

Conclusions

Overall, six studies (Desrochers-Couture et al. 2018; Min et al. 2009; Braun et al. 2012; Kordas et al. 2011; Schnaas et al. 2006; Taylor et al. 2017) have been published that could potentially meet the inclusion criteria for the original analysis conducted by Lanphear et al. (2005). The blood lead concentrations were higher than Flint children in four of these studies (Min et al. 2009; Braun et al. 2012; Kordas et al. 2011; Schnaas et al. 2006) and two of the studies featured cohorts with low BLL that are comparable to Flint children (Taylor et al. 2017; Desrochers-Couture et al. 2018). Among the studies with low lead blood levels, comparable to those measured among Flint children during the water crisis, there was no evidence of an association with decrements in cognitive function.

Conclusion

The current position held by the CDC and the NTP are driven by the literature, but focus primarily on a pooled analysis of seven longitudinal cohort studies (Lanphear et al. 2005). As described above, there is possible exposure misclassification for over 20% of the children identified as having low BLL (e.g. < 10 µg/dL). Even if these discrepancies are not taken into account, a re-evaluation of that pooled analysis demonstrates that it is impossible to evaluate the impact of low BLL on cognition for concurrent BLL that are under 6 µg/dL (Crump et al. 2013). Even when the potential for exposure misclassification is not taken into consideration, only 8% of the children in the pooled analysis had BLL < 7.5 µg/dL and no data was provided on the prevalence of children with peak exposures < 5 µg/dL. Approximately 82% of the children included in these analyses had peak BLL that exceeded 10 µg/dL. Very few studies exist that focus solely on children with peak blood lead exposure data less than 5 µg/dL.

Furthermore, the more recently published longitudinal cohort studies show that there is not a relationship between low BLL and decrements in cognitive outcomes, when BLL more closely match Flint children.

Due to the paucity of data available for children with BLL < 5 µg/dL, the scientific evidence does not support a causal association between that concentration of lead in the blood and decreases in IQ.

2.5 THERE IS NO SCIENTIFIC EVIDENCE THAT LOW PRENATAL LEAD EXPOSURE (MEASURED AT CONCENTRATIONS ≤ 5 µg/dL) LEADS TO A REDUCTION IN IQ.

There are several measures of cognitive function, which includes intelligence quotient (IQ), academic performance and achievement, as well as general and specific cognitive abilities (ATSDR 2020; EPA 2013; NTP 2012a, 2012b). Mental development in infants between 6 months to 3 years has been assessed with the Mental Development Index (MDI) of the Bayley Scales of Infant Development. As noted by the US EPA, the MDI test is not an intelligence test, and scores from the MDI test, especially before 2 to 3 years of age, are not "necessarily strongly correlated with later measurements of FSIQ in children" (EPA 2013, p. 721). Additionally, studies evaluating learning and memory have employed a variety of metrics, leading to heterogeneity across studies, which results in challenges when comparing and synthesizing findings across studies (EPA 2013). Cognitive development, namely IQ, is assessed in children by Full Scale Intelligence Quotient (FSIQ), has "strong psychometric properties (i.e., reliability, consistency, validity), is among the most rigorously standardized cognitive measures, is relatively stable in school-age, and has been predictive of educational achieve and life success" (EPA 2013, p. 703). For these reasons, IQ, as measured via versions of the Wechsler Pre-school and Primary Scale of Intelligence and the Wechsler Intelligence Scale for Children were considered for inclusion in the below evaluation.

A review of the literature was conducted to identify longitudinal studies that evaluated prenatal lead levels and IQ decrements in childhood. Studies evaluating measures of cognitive function other than IQ (e.g., MDI) were excluded from this review. In order to identify papers on cognitive function, and namely intelligence quotient (IQ), an initial review of governmental reports (i.e., ATSDR 2020; EPA 2013; NTP 2012b) was conducted to identify primary sources. Once the governmental documents and the primary sources were reviewed, an independent literature search was performed in PubMed. A total of 10 studies were identified where central tendency of exposure was ≤ 10 µg/dL and are reviewed below (Baghurst et al. 1992; Desrochers-Couture et al. 2018; Dietrich et al. 1993; Ernhart et al. 1989; Schnaas et al. 2006; Taylor et al. 2017; Tong et al. 1996; Wasserman et al. 1997; Wasserman et al. 2000; Winneke et al. 1985).

Results of Populations with Prenatal Exposures <5 µg/dL

There were two studies that were identified that evaluated IQ deficits among children who had prenatal lead levels <5 µg/dL (Desrochers-Couture et al. 2018; Taylor et al. 2017).

Taylor et al. (2017) conducted a prospective cohort study to examine prenatal and 30-month postnatal blood lead measurements and child IQ scores to determine whether there were sex differences in the influence of lead exposure on IQ, and to determine the moderation effect of prenatal lead exposure on child IQ. The cohort included mother-infant pairs from the United Kingdom who were enrolled in the population-based Avon Longitudinal Study of Parents and Children (ALSPAC) and born between April 1991 and December 1992. Among the 4,316 live births, 348 children had complete data at the age four measurement, and 1,826 (1,823 for total IQ only) had complete data at the age eight measurement. Maternal blood samples were collected at a median gestational age of 11 weeks (IQR: 9–13 weeks) and the arithmetic mean prenatal blood lead levels were 3.67 (SD: 1.46, median: 3.41, range 0.20–19.14) µg/dl, with 14.3% of women having prenatal blood lead levels < 5 µg/dl. The mean blood lead levels at 30 months were 4.22 (SD: 3.12) µg/dl. Full IQ testing was conducted among a random subsample (10%) of children at 4 years of age using the Wechsler Pre-school and Primary Scale of Intelligence –

Revised UK edition (WPPSI), and from all children at age 8 years using the Wechsler Intelligence Scale for Children (WISC-III). Logistic regression analysis was used to examine the effect of prenatal blood lead of ≤ 5ug/dl on the likelihood of being in the lowest IQ quartile compared with the highest three quartiles. Confounders considered included family adversity index, housing tenure, household crowding, smoking in the first trimester, alcohol consumption in the first trimester, maternal age at index birth, parity, maternal education, length of time the mother had lived in Avon, child sex, child age at testing, weighted life events score and hemoglobin (Hb) level. Univariate and multivariable linear regression models were used to examine the association of prenatal blood lead with verbal, performance and total IQ at age 4 and age 8 years They found no evidence supporting an association between moderate to low prenatal blood levels in the first trimester with child IQ at age 4 or 8 years of age in the adjusted regression models and no moderation of the association between child blood lead and IQ. In girls only, there was a statistically significant positive association between verbal IQ and total IQ at age 8, such that each 1 µg/dL increase prenatal blood lead concentration was associated with a 0.71 points higher verbal IQ score (95% CI: 0.11 to 1.32; p=0.021) and a 0.73 points higher total IQ score (95% CI: 0.13-1.33; p=0.017). Conversely, the coefficients tended to be negative in boys (-0.15, -0.42, and -0.29 points, respectively), although none of the associations were statistically significant.

Desrochers-Couture et al. (2018) examined a cohort of pregnant women who were recruited between 2001 and 2008 from various Canadian cities as part of the Maternal-Infant Research on Environmental Chemicals (MIREC) Study. In a subset of 609 children, mean (SD) lead levels from blood during the 1st and 3rd trimester, umbilical cord, and children's blood between ages 3 and 4 were 0.62 (1.6), 0.59 (1.7), 0.76 (1.7), and 0.7 (1.7), respectively. Cognitive function was measured with the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III) between ages 3 and 4. After adjusting for child age, child sex, maternal education, evaluation site, cord blood mercury, marital status, familial income, HOME score, and parenting stress index, there were no significant associations between maternal blood lead, cord blood lead, or child blood lead levels and intellectual scores ($p > 0.05$). The authors did test for effect modification between sex and blood lead levels and found a significant effect for males ($\beta = -3.28$; 95% CI: -5.31, -1.18) on cord blood levels and IQ. Overall, no statistically significant associations between prenatal, cord blood, and child blood lead levels and intellectual function were found, but there was statistically significant sex-linked effect modification for a negative effect on performance IQ in males.

Results of Populations with Prenatal Exposures < 10 µg/dL

Based on the review of governmental documents and an independent literature search, a total of eight studies were identified that evaluated prenatal lead exposures and associations with childhood IQ where the central tendency of BLL was greater than 5 but less than 10 µg/dL. These studies were conducted in Port Pirie, Australia (Baghurst et al. 1992; Tong et al. 1996), Kosovo, Yugoslavia (Wasserman et al. 1997; Wasserman et al. 2000), Mexico City, Mexico (Schnaas et al. 2006), Nordenham, Germany (Winneke et al. 1985), Cincinnati, OH (Dietrich et al. 1993), and Cleveland, OH (Ernhart et al. 1989).

The Yugoslavia Prospective Study was initiated among 1,502 women who were pregnant between 1984 and 1985 in two towns in Kosovo, including Mictrovica, which has a lead smelter, finery, and battery factory, as well as Pristina, which has no known lead exposures (Wasserman et al. 1997; Wasserman et al. 2000). Blood lead levels were measured mid-pregnancy and then at 6-month intervals from birth until the children were approximately 7 years of age. Among children with complete data at age 7, the mean (SD) blood lead levels at mid-pregnancy were 5.6 (2.0) and 20.8 (7.9) µg/dL in Pristina and Mitrovica, respectively, and the umbilical cord lead levels

were 5.7 (3.6) and 23.2 (8.2) µg/dL in Pristina and Mitrovica, respectively (Wasserman et al. 1997). Intelligence was measured at age 5 with the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R), and at age 7 with the Wechsler Intelligence Scale for Children-Version III (WISC-III). In the initial study, Wasserman et al. (1997) examined the association between lead exposure and IQ at age 7. However, blood lead levels were analysed as a cumulative lifetime lead exposure variable, and there were no results specific to prenatal lead exposures. Wasserman et al. (2000) conducted an update on the 1997 analysis with the objective of describing separate associations with prenatal and postnatal lead exposures. In this update, a prenatal lead exposure variable was calculated as the mean of the mid-pregnancy and delivery blood lead levels. Adjustments were made for maternal age, HOME score, child's age at time of intelligence test, child's sex, birthweight, ethnicity, years of maternal education, maternal Raven's score, and number of previous live births. Notably, separate analyses were not conducted by town, and the analyses represents the overall population. BLLs were $\log_{10}$ transformed the mean (SD) $\log_{10}$ mid-pregnancy and umbilical cord blood lead levels for Mictrovica and Pristina combined were 1.00 µg/dL (0.32) and 1.01 µg/dL (0.36), respectively. The mean $\log_{10}$ BLL's are equivalent to BLL's of 10.0 and 10.2 µg/dL, respectively. After adjustment for covariates, there was a statistically significant decrease of 6.05 IQ points (SE: 1.35, $p<0.001$) for each log unit increase in prenatal BLL, representing a 1.07 IQ point decrease (95% CI: 0.60, 1.53) for each 50% increase in prenatal BLL. Adjusting for covariates and prenatal BLL, there was a statistically significant decrease in IQ associated with postnatal BLL increases occurring in either the late and/or early postnatal periods ($p<0.05$). A 50% increase in both early and late postnatal BLL relative to prenatal BLL was associated with a 2.71 IQ point decrease (95% CI: -4.91, -0.52), and a 50% increase in only the late postnatal BLL relative to prenatal BLL was associated with a 1.78 IQ point decrease (95% CI: -3.51, -0.05). The authors concluded that increases in prenatal and postnatal blood lead levels were independently associated with small decreases in children's intelligence.

Schnaas et al. (2006) conducted a prospective cohort study of children born in Mexico City, Mexico, between 1987 and 1992 to characterize the association between prenatal and postnatal lead exposure with intellectual development. Prenatal blood lead levels were measured at 12, 20, 28, and 36 weeks of pregnancy, cord BLL was measured at delivery, and child BLLs were measured every 6 months after birth to age 5 and then annually from ages 6 to 10. The geometric mean (range) during pregnancy was 8.0 µg/dL (1-33), 9.8 µg/dL (2.8-36.4) from 1-5 years, and 6.2 µg/dL (2.2-18.6) from 6-10 years. The Spanish version of the Wechsler Intelligence Scale for Children–Revised (WISC-R) was administered annually between ages 6 to 10 years in order to obtain a full-scale IQ (FSIQ) score. Linear mixed models with random intercept and slope were utilized to analyze the pattern of blood lead level effects on FSIQ from 6 to 10 years of age, controlling for maternal IQ, child's sex, SES, birth weight, and HOME score. Results indicated that mothers with higher blood lead levels during the third trimester (i.e., geometric mean of maternal lead levels at 28 and 36 weeks) had children with statistically significantly lower FSIQ scores ($\beta = -3.90$, 95% CI: -6.45, -1.36) at 6 to 10 years of age. In order to more precisely evaluate which prenatal lead levels were associated with subsequent IQ decrements, similar analyses were conducted for each of the prenatal BLL measurements at 12, 20, 28, and 36 weeks of pregnancy, which demonstrated that only BLL at week 28 of pregnancy was statistically significantly associated with FSIQ scores ($\beta = -4.13$, 95% CI: -6.45, -1.81). The authors concluded that maternal blood lead levels during the third trimester of pregnancy, especially around week 28, were associated with decreased intellectual development in children.

Dietrich et al. (1993) evaluated IQ at 6.5 years of age among 253 children from the Cincinnati Lead Study Cohort. Blood lead concentrations were measured in the first trimester of pregnancy, at approximately 10 days old from infants, and then at quarterly intervals until age 5 and at 5.5

years, 6 years, and 6.5 years. Mean (SD) prenatal blood lead levels in mothers was 8.3 (3.7) µg/dl and in newborns 5 (3.4) µg/dl, and blood lead levels in the children peaked around 2 years of age and graduated declined thereafter. The WISC-R was administered at approximately 6.5 years of age to obtain FSIQ. Multiple linear regression was conducted that adjusted for HOME score, maternal IQ, birth weight and length, child sex, and cigarette consumption during pregnancy. After adjustment, prenatal lead exposures were unrelated to FSIQ at age 6.5 years. The interaction of lead exposure with gender and social class was also examined, which was also not statistically significant after covariate adjustment.

Winneke et al. (1985) evaluated IQ in a sample of 114 six- and seven-year-old children who were born between July 1975 and August 1976 and living in Nordenham, Germany, a town with a lead-zinc smelter as the largest industrial complex. The mean (SD) maternal and cord blood lead levels, respectively, were 9.3 µg/dl (range: 4-30) and 8.2 µg/dl (range: 4-31). The WISC test was administered at age 7 to obtain a FSIQ score. Stepwise multiple-regression analysis was conducted and included the following covariates: sex, and other factors covering social and family background and medical history. The results of this analysis demonstrated that there were no statistically significant associations between maternal and cord lead levels with FSIQ scores at age 7.

In a prospective cohort study, Ernhart et al. (1989) evaluated the associated between prenatal lead exposure and IQ measured between ages 4 and 5 years (mean age: 4.8 years) among 165 children in Cleveland, OH. The initial recruitment occurred at the mother's first antenatal visit to clinics and the infants of all women in the antenatal study who were born in a fifteen-month period were considered for selection in the study. Blood samples were collected from mothers at delivery, as well as cord blood samples and blood samples at 6 months, 2 years, and three years from the children. The arithmetic mean (SD) maternal and cord blood lead levels, respectively, were 6.50 µg/dl (1.84) and 5.89 µg/dl (2.10). Intelligence was assessed via the WPPSI at 4 years, 10 months old. Linear regression analysis was conducted, adjusting for relevant covariates, such demographic and perinatal variables, and the HOME score. After adjustment for covariates, there were no statistically significant effects between prenatal lead exposure and FSIQ in this study.

Conclusion

A review of the literature on prenatal and cord blood measures with central tendency of exposure measures at < 5 µg/dL found no statistically significant associations between maternal blood lead levels and childhood cognition measured as full scale IQ. This literature review was then expanded to include additional studies where the central tendency of exposure was measured to be > 5 µg/dL and < 10 µg/dL. Of the eight additional papers, only two studies observed statistically significant associations. However, Wasserman et al. (2000) included a cohort of women with blood lead levels at mid-pregnancy of 20.8 (7.9) µg/dL. Analyses were not conducted in the comparison cohort only, where blood lead levels at mid-pregnancy were 5.6 (2.0) µg/dL. These measures far exceed the mean measured in women of childbearing age in Flint (0.69 µg/dL) as reported by Gomez et al. 2019b). Schnaas et al. (2006) also demonstrated a statistically significant association between prenatal levels and childhood IQ. Nevertheless, the five remaining studies where central tendency values were measured above 5 µg/dL failed to observe a statistically significant association between prenatal measures of blood lead and IQ. There is no evidence that at low levels of exposure (prenatal BLL < 5 µg/dL) are associated with decrements in cognition during childhood.

2.6 No Causal Associations Can be Established Between Maternal or Umbilical Cord Blood Levels ≤ 5 µg/dL and Birth Weight, Gestation Age (or Preterm Birth), and Small for Gestational Age.

A review of the literature was conducted to identify longitudinal studies that evaluated low-level prenatal lead exposures and three developmental or birth outcomes (i.e., birth weight, gestational age/preterm birth, and small for gestational age). Preterm births are defined as live births that occur prior to 37 weeks of gestation. Small for gestational age is an evaluation of size/growth after accounting for the duration of gestation. In order to identify papers on specific birth outcomes, an initial review of governmental reports (i.e., ATSDR 2020; EPA 2013; NTP 2012b was conducted to identify primary sources). Only studies in populations with a reported central tendency (mean, geometric mean, or median) for maternal or umbilical cord blood lead levels of ≤ 5 µg/dL were considered for inclusion. The results by specific outcome are described below.

Birth Weight

Overall, 22 studies with a birth weight outcome met these criteria (Table 2). Nine of these studies were conducted in North America (8 in the US and 1 in Canada), six were conducted in Europe (1 each in Spain, Austria, Sweden, and the UK, and 2 in Norway & Russia), five were conducted in Asia (1 each in Korea and Japan, and 3 in China), one study was conducted in Brazil, and one in Saudi Arabia. Most of the studies had between 100 and 1000 participants (n=13; 59.1%), but three studies had populations of less than 100 mother/child pairs. Half of the studies were cross-sectional (n=11), one was a case-control study, and the remainder had a cohort design (n=10; 45.5%). Three of the studies measured maternal blood lead levels multiple times during pregnancy, seven measured maternal blood lead levels once during pregnancy, and four studies measured maternal blood lead levels at delivery only. The 8 studies that collected umbilical cord blood lead did so during delivery.

The mean umbilical cord measures (n=8) ranged from 0.84 µg/dL (Wells et al. 2011) to 4.9 µg/dL (Satin et al. 1991), with two studies reporting medians of 1.12 µg/dL (Osman et al. 2000) and 1.3 µg/dL (Gundacker et al. 2010), and two studies reporting geometric means of 4.07 µg/dL (Wang et al. 2017c) and 1.3 µg/dL (Jones et al. 2010). The mean maternal blood measures (n=14) ranged from 0.42 µg/dL measured during the 2nd trimester (Rabito et al. 2014) to 3.67 µg/dL measured at birth (Taylor et al. 2015; Taylor et al. 2013), with two studies reporting medians of 2.1 µg/dL (Odland et al. 2004) and 2.5 µg/dL (Gundacker et al. 2010) and one study reporting a geometric mean of 1.83 µg/dL (Garcia-Esquinas et al. 2014). Nine of the 22 studies (40.9%) found statistically significant associations between maternal or umbilical cord blood lead and birth weight. Of these 9 studies, two found statistically significant associations for male infants but not for female infants between maternal blood lead levels (Nishioka et al. 2014) or umbilical cord lead levels (Wang et al. 2017c) and birth weight. The studies by Taylor et al (2015; 2013) stratified their analyses where mothers with blood lead levels of < 5 µg/dL were the referent group. This indicates that any findings do not pertain to these low blood level referent births. Additionally, Zentner et al. (2006) did not adjust their models for potential confounding factors. The majority of studies (n=13) demonstrated that maternal blood lead or umbilical cord blood measures were not associated with birth weight.

Table 2. Studies on Low-Level Prenatal Lead Exposure (≤5 µg/dL) and Birth Weight

Source	Study	Study location	Study design; Sample size	BLL measure and timing	Statistically significant finding?	Adjusted analysis?
ATSDR (2020)[a]	Al-Saleh et al. (2014)	Saudi Arabia	Cross-sectional; n=1,578	Mean (SD) maternal BLL hours after delivery: 2.897 (1.851) µg/dL	No	Yes
ATSDR (2020)[a]	Bloom et al. (2015)	United States	Case-control; n=235	Mean (SD) maternal BLL (2nd or 3rd trimester): 0.71 (0.30) µg/dL	No	Yes
ATSDR (2020)[a]	Garcia-Esquinas et al. (2014)	Spain	Birth cohort; n=100	Geo mean maternal BLL (at a median of 33.9 weeks): 1.83 (95% CI: 1.67-2.01) µg/dL	No	Yes
EPA (2013)[c], NTP (2012b)[b]	Gundacker et al. (2010)	Austria	Cohort; n=53	Median (IQR) maternal BLL between week 34-38: 2.5 (1.8-3.5) µg/dL, median (IQR) cord BLL: 1.3 (0.8-2.4) µg/dL	No*	Yes
EPA (2013)[c], NTP (2012b)[b]	Jones et al. (2010)	United States	Cross-sectional; n=102	Mean (SD) cord BLL: 2.4 (4.3) µg/dL, geo mean cord BLL: 1.3 µg/dL	No	No
ATSDR (2020)[a]	Kim et al. (2017)	Korea	Longitudinal cohort; n=280	Mean (SE) cord BLL: 1.31 (0.06) µg/dL	No	Yes
ATSDR (2020)[a]	Nishioka et al. (2014)	Japan	Cohort; n=386	Maternal (SD) BLL at 12 weeks: 0.98 (0.55) µg/dL, at 25 weeks: 0.92 (0.63) µg/dL, at 36 weeks: 0.99 (0.66) µg/dL	Yes for male infants; no for female infants	Yes
ATSDR (2020)[a], NTP (2012b)[b]	Odland et al. (1999)	Norway and Russia	Cross-sectional; n=262	Mean (range) maternal BLL collected at delivery in Russian cohort: 2.9 (0.83-13.5) µg/dL, in Norwegian cohort: 2.3 (0.41-3.9) µg/dL	Yes	Yes
NTP (2012b)[b]	Odland et al. (2004)	Norway and Russia	Cross-sectional; n=262	Median (range) maternal BLL collected at delivery: 0.1 (0.02-0.65) µmol/L	No	Yes

Source	Study	Study location	Study design; Sample size	BLL measure and timing	Statistically significant finding?	Adjusted analysis?
NTP (2012b)[b]	Osman et al. (2000)	Sweden	Cross-sectional; n=106	Median cord BLL: 1.12 µg/dL	Yes	Yes
ATSDR (2020)[a]	Perkins et al. (2014)	United States	Birth cohort; n=829	Mean (SD) maternal RBC BLL (at a mean of 27.9 weeks): 1.22 (0.59) µg/dL	No	Yes
ATSDR (2020)[a]	Rabito et al. (2014)	United States	Birth cohort; n=98	Mean (SD) maternal 2nd trimester BLL: 0.42 (0.20) µg/dL; 3rd trimester: 0.45 (0.28) µg/dL; delivery: 0.50 (0.35) µg/dL	No	Yes
NTP (2012b)[b]	Rhainds et al. (1999)	Canada	Cross-sectional; n=1,109	Cord BLL: 1.57 µg/dL	No	Not specified
NTP (2012b)[b]	Satin et al. (1991)	United States	Cross-sectional; n=723	Cord BLL: 4.9 µg/dL	No	Yes
NTP (2012b)[b]	Sowers et al. (2002)	United States	Cross-sectional; n=705	Mean (SD) maternal BLL at 12 weeks: 1.2 (0.03) µg/dL, at 20 weeks: 1.08 (0.05) µg/dL, at 28 weeks: 1.10 (0.03) µg/dL, at birth: 1.32 (0.03) µg/dL	No	Yes
ATSDR (2020)[a]	Taylor et al. (2015); (2013)(two studies on the same cohort)	United Kingdom	Longitudinal cohort; n=4,285	Mean (SD) maternal BLL (at a median of 11 weeks): 3.67 (1.47) µg/dL	Yes, however population stratified by < 5.0 and ≥ 5.0 µg/dL	Yes
ATSDR (2020)[a]	Wang et al. (2017b)	China	Prospective cohort; n=3,125	Mean (range) maternal serum Pb (1ST or 2nd trimester): 1.50 (0.02-5.46) µg/dL	Yes	Yes

Source	Study	Study location	Study design; Sample size	BLL measure and timing	Statistically significant finding?	Adjusted analysis?
ATSDR (2020)[a]	Wang et al. (2017c)	China	Cross-sectional; n=1,009	Geo mean cord BLL: 4.07 (95% CI: 3.89-4.17) µg/dL	No for all Yes for male infants; no for female infants	Yes
EPA (2013)[c]	Wells et al. (2011)	United States	Cross-sectional; n=300	Mean cord BLL 0.84 (95% CI: 0.72-0.96) µg/dL	No	Yes
ATSDR (2020)[a]	Xie et al. (2013)	China	Birth cohort; n=252	Mean (SD) maternal BLL at delivery: 3.53 (1.51) µg/dL	Yes	Yes
EPA (2013)[c], NTP (2012b)[b]	Zentner et al. (2006)	Brazil	Cross-sectional; n=55	Mean (SD) cord BLL 3.9 (3.6) µg/dL	Yes	No
ATSDR (2020)[a], EPA (2013)[c], NTP (2012b)[b]	Zhu et al. (2010)	United States	Retrospective cohort; n=43,288	Mean (range) maternal BLL taken a mean of 203 days before birth: 2.1 (0 – 9.9) µg/dL	Yes	Yes

* The NTP Monograph states that there is a statistically significant association reported in Gundacker et al. 2010, and the EPA ISA document does not. The source manuscript states a p-value of 0.058 for maternal blood lead in an adjusted model for the birth weight outcome.
[a] ATSDR, Table 2-41. Summary of Epidemiological Studies Evaluating Birth Outcomes Effects of Mean Blood Lead Concentration ≤ 10 µg/dL (and Supporting Document Table 13)
[b] NTP, Appendix E: Human Studies of Reproductive and Developmental Effects of Pb Considered in Developing Conclusions
[c] EPA ISA, Table 4-42: Summary of epidemiologic studies of associations between Pb exposure indicators and low birth weight and fetal growth

Gestational Age / Preterm Birth

Fifteen studies with a gestational age or preterm birth outcome met our inclusion criteria (Table 3). The majority of these studies were conducted in the US (n=8; 53.3%), four studies were conducted in Europe (1 in Poland and Sweden, 1 in Spain, 1 in the UK, and 1 in Norway and Russia), one each were conducted in China, India, and Iran. Most of the studies had fewer than 1,000 participants (n=12; 80.0%) and the smallest study only had 30 mother/child pairs (Fagher et al. 1993). There were 7 cross-sectional studies, 7 cohort studies, and 1 study of case-control design. Two of the studies measured maternal blood lead levels multiple times during pregnancy, seven measured maternal blood lead levels once during pregnancy, and two studies measured maternal blood lead levels at delivery only. The 4 studies that only collected umbilical cord blood lead did so during delivery.

The mean umbilical cord measures (n=4) ranged from 0.84 µg/dL (Wells et al. 2011) to 4.9 µg/dL (Satin et al. 1991). The mean maternal blood measures (n=11) ranged from 0.42 µg/dL measured during the 2nd trimester (Rabito et al. 2014) to 4.52 µg/dL measured in the sub-population of preterm births (Vigeh et al. 2011), with one study reporting medians of 2.9 µg/dL and 1.24 µg/dL (Odland et al. 1999; Russian and Norwegian cohorts, respectively) and one study reporting a geometric mean of 1.83 µg/dL (Garcia-Esquinas et al. 2014). Seven of the 15 studies (46.7%) found statistically significant associations between maternal or umbilical cord blood lead and gestational age or preterm birth. Of these 7 studies, one did not provide effect estimates or 95% confidence intervals nor did they specify if models were adjusted for potential confounding factors (Patel and Prabhu 2009). Over half of the studies failed to demonstrate an association between maternal blood lead or umbilical cord blood measures and gestations age or preterm birth.

Table 3. Studies on Low-Level Prenatal Lead Exposure (≤5 µg/dL) and Gestational Age/Preterm Birth

Source	Study	Study location	Study design; Sample size	BLL measure and timing	Statistically significant finding?	Adjusted analysis?
ATSDR (2020)[a]	Bloom et al. (2015)	United States	Case-control; n=235	Mean (SD) maternal BLL (2nd or 3rd trimester): 0.71 (0.30) µg/dL	No	Yes
NTP (2012b)[b]	Fagher et al. (1993)	Poland and Sweden	Cross-sectional; n=30	Mean (SD) maternal BLL (at delivery) preterm: 3.16 (1.94) µg/dL; term: 3.37 (1.88) µg/dL	No	Not specified
ATSDR (2020)[a]	Garcia-Esquinas et al. (2014)	Spain	Birth cohort; n=100	Geo mean maternal BLL (at a median of 33.9 weeks): 1.83 (95% CI: 1.67-2.01) µg/dL	No	Yes
EPA (2013), NTP (2012b)[b]	Jones et al. (2010)	United States	Cross-sectional; n=102	Mean (SD) cord BLL: 2.4 (4.3) µg/dL; geo mean cord BLL: 1.3 µg/dL	No	No
ATSDR (2020)[a]	Li et al. (2017)	China	Birth cohort; n=3,125	Mean (range) maternal BLL (at a median of 14 weeks): 1.5 (0.02-5.46) µg/dL	Yes (preterm birth)	Yes
NTP (2012b)[b]	Odland et al. (1999)	Norway and Russia	Cross-sectional; n=262	Mean (range) maternal BLL collected at delivery in Russian cohort: 2.9 (0.83-13.5) µg/dL, in Norwegian cohort: 2.3 (0.41-3.9) µg/dL	Yes (gestational age)	Yes
EPA (2013)[c]	Patel and Prabhu (2009)	India	Cross-sectional; n=205	Mean (SD) cord BLL: 4.7 (12.1) µg/dL	Yes (length of gestation), but no effect measure or 95% CI given	Not specified

Source	Study	Study location	Study design; Sample size	BLL measure and timing	Statistically significant finding?	Adjusted analysis?
ATSDR (2020)[a]	Perkins et al. (2014)	United States	Birth cohort; n=949	Mean (SD) maternal RBC BLL (at a mean of 27.9 weeks): 1.22 (0.59) µg/dL	No	Yes
ATSDR (2020)[a]	Rabito et al. (2014)	United States	Birth cohort; n=98	Mean (SD) maternal 2nd trimester BLL: 0.42 (0.20) µg/dL; 3rd trimester: 0.45 (0.28) µg/dL; delivery: 0.50 (0.35) µg/dL	Yes (preterm birth)	Yes
NTP (2012b)[b]	Satin et al. (1991)	United States	Cross-sectional; n=723	Cord BLL: 4.9 µg/dL	Yes (preterm birth)	Yes
NTP (2012b)[b]	Sowers et al. (2002)	United States	Cross-sectional; n=705	Mean (SD) maternal BLL at 12 weeks: 1.2 (0.03) µg/dL, at 20 weeks: 1.08 (0.05) µg/dL, at 28 weeks: 1.10 (0.03) µg/dL, at birth: 1.32 (0.03) µg/dL	No	Yes
ATSDR (2020)[a]	Taylor et al. (2015); (2013) (two studies on the same cohort)	United Kingdom	Longitudinal cohort; n=3,870	Mean (SD) maternal BLL (at a median of 11 weeks): 3.67 (1.47) µg/dL	Yes (preterm birth), however population stratified by < 5.0 and ≥ 5.0 µg/dL	Yes
ATSDR (2020)[a], EPA (2013)[c], NTP (2012b)[b]	Vigeh et al. (2011)	Iran	Longitudinal cohort; n=348	Mean (SD) maternal BLL during 1st trimester: 3.8 (2.0) µg/dL	Yes (preterm birth)	Yes

Source	Study	Study location	Study design; Sample size	BLL measure and timing	Statistically significant finding?	Adjusted analysis?
EPA (2013)[c]	Wells et al. (2011)	United States	Cross-sectional; n=300	Mean cord BLL: 0.84 (95% CI: 0.72-0.96)	No	Yes
ATSDR (2020)[a], EPA (2013)[c], NTP (2012b)[b]	Zhu et al. (2010)	United States	Retrospective cohort; n=43,288	Mean (range) maternal BLL taken a mean of 203 days before birth: 2.1 (0 – 9.9) µg/dL	No	Yes

[a] ATSDR, Table 2-38. Summary of Epidemiological Studies Evaluating Effects on the Female Reproductive System at Mean Blood Lead Concentration ≤ 10 µg/dL (and Supporting Document Table 12)
[b] NTP, Appendix E: Human Studies of Reproductive and Developmental Effects of Pb Considered in Developing Conclusions
[c] EPA ISA, Table 4-41: Summary of recent epidemiologic studies of associations between Pb exposure indicators and preterm birth

Small for Gestational Age

Six studies investigated the relationship between maternal blood lead levels and the birth outcome of small for gestational age (Table 4). Four of these studies were conducted in North America (2 in the US, 1 in Canada, and 1 in Mexico), 1 was conducted in China, and 1 in Saudi Arabia. All of the studies were relatively large, with the smallest study population being 705 and the largest being over 43,000. Four of the studies had a cohort design and 2 of them were cross-sectional. Two studies collected maternal blood once during pregnancy, one study collected maternal blood twice during pregnancy, and one hours after delivery. A fifth study collected maternal blood multiple times during pregnancy as well as at delivery. The sixth study was a linked records study, where the maternal blood lead levels were taken a mean of 203 days before delivery. The mean maternal blood measures ranged from 1.08 µg/dL at 20 weeks of gestation (Sowers et al. 2002) to 3.7 µg/dL in the 2nd trimester (Rodosthenous et al. 2017), with one study reporting a median of 0.59 µg/dL (Thomas et al. 2015). Only one of the 6 studies (16.7%) found a statistically significant association between maternal blood lead and small for gestational age. This was a cohort study on a Chinese population where maternal blood was collected in the 1st or 2nd trimester of pregnancy (Wang et al. 2017b).

The inconsistent findings of studies on populations with low level blood lead measures (≤ 5 µg/dL), make it impossible to form a concrete conclusion on a causal relationship between low level blood lead as measured in umbilical cord or maternal blood lead and the birth outcomes of birth weight and length of gestation. The three large review documents examined here do not agree on their conclusions for birth weight and growth outcomes. Although the authors of the NTP Monograph stated that “[t]here is sufficient evidence that maternal blood Pb levels < 5 µg/dL are associated with reduced fetal growth and lower birth weight” in 2012 (p. 109), the authors of the EPA ISA for Lead noted less consistency in results in studies of maternal and cord blood lead with these outcomes (p. 4-655) in 2013, and the authors of the ATSDR Toxicological Profile for Lead stated in 2020 that effects on birth outcomes including decreased birth weight were mixed across studies at blood lead levels ≤ 10 µg/dL (p. 219). There is more agreement in their conclusions regarding gestational age or preterm birth. The NTP Monograph states that "[t]here is limited evidence that maternal blood Pb levels < 10 µg/dL are associated with preterm birth or reduced gestational age, because of inconsistent results in studies with low blood Pb levels." (p. 112), the authors of both the EPA Integrated Science Assessment and the ASTDR Toxicological Profile for lead observed mixed results for preterm birth (p. 4-630 and p. 217, respectively).

Table 4. Studies on Low-Level Prenatal Lead Exposure (≤5 µg/dL) and Small for Gestational Age

Source	Study	Study location	Study design; Sample size	BLL measure and timing	Statistically significant finding?	Adjusted analysis?
ATSDR (2020)[a]	Al-Saleh et al. (2014)	Saudi Arabia	Cross-sectional; n=1,578	Mean (SD) maternal BLL hours after delivery: 2.897 (1.851) µg/dL	No	Yes
ATSDR (2020)[a]	Rodosthenous et al. (2017)	Mexico	Prospective cohort; n=944	Mean (SD) maternal 2nd trimester BLL: 3.7 (2.7) µg/dL	No	Yes
NTP (2012b)[b]	Sowers et al. (2002)	United States	Cross-sectional; n=705	Mean (SD) maternal BLL at 12 weeks: 1.2 (0.04) µg/dL, at 20 weeks: 1.08 (0.05) µg/dL, at 28 weeks: 1.10 (0.03) µg/dL, at birth: 1.32 (0.03) µg/dL	No	Yes
ATSDR (2020)[a]	Thomas et al. (2015)	Canada	Prospective cohort; n=1,835	Median (range) maternal BLL (average of 1st and 3rd trimester sample): 0.59 (0.17-4.04) µg/dL	No	Yes
ATSDR (2020)[a]	Wang et al. (2017b)	China	Prospective cohort; n=3,125	Mean (range) maternal serum Pb (1ST or 2nd trimester): 1.50 (0.02-5.46) µg/dL	Yes	Yes
ATSDR (2020)[a], EPA (2013)[c], NTP (2012b)[b]	Zhu et al. (2010)	United States	Retrospective cohort; n=43,288	Mean (range) maternal BLL taken a mean of 203 days before birth: 2.1 (0 – 9.9) µg/dL	No	Yes

[a] ATSDR, Table 2-41. Summary of Epidemiological Studies Evaluating Birth Outcomes Effects of Mean Blood Lead Concentration ≤ 10 µg/dL (and Supporting Document Table 13)
[b] NTP, Appendix E: Human Studies of Reproductive and Developmental Effects of Pb Considered in Developing Conclusions
[c] EPA ISA, Table 4-42: Summary of epidemiologic studies of associations between Pb exposure indicators and low birth weight and fetal growth

Conclusion

The currently available literature on low BLL and these birth outcomes is not consistent. One of the key tenants to causality is consistency in findings across studies. The research is more likely to demonstrate no association between low BLL and SGA with only one study reporting a statistically significant association. The findings for gestational age/preterm birth and for birth weight are equivocal without convincing evidence one way or another regarding a potential association with these outcomes and low BLL exposures. The scientific literature does not support a causal association between low BLL and these birth outcomes.

2.7 THERE IS NO SCIENTIFIC EVIDENCE THAT LOW CHILDHOOD EXPOSURES TO LEAD (MEASURED AS BLOOD LEAD LEVEL ≤ 5 µG/DL) LEADS TO REDUCED COGNITIVE FUNCTION IN ADULTHOOD

I conducted a systematic literature review to identify papers that could provide evidence, or lack thereof, of an association between exposure to lead and adult cognitive outcomes for exposures comparable to those experienced by children in Flint.

Literature Review Methods

The initial phase of the review focused on a few key source documents, which included the Toxicological Profile for Lead published by the Agency for Toxic Substances and Disease Registry (ATSDR 2020), the NTP Monograph: Health Effects of Low-Level Lead (NTP 2012b), and a review paper authored by Shih et al. (2007). Due to the paucity of identified studies, two independent searches were conducted with PubMed. The first search was conducted with the following search query: ("childhood lead" OR "childhood blood lead" OR "children lead" OR "childhood bone lead" OR "childhood lead exposure" or "children blood lead levels") AND ("cognitive outcomes" OR "neurological outcomes" OR "IQ") AND ("adult" OR "teenage" OR "young adult"). Bone lead measures were subsequently excluded from our review criteria because reference levels of bone lead in children and associated health effects are unknown. A second search was used to identify studies with relevant exposures, and included the search terms: "childhood blood lead levels," "childhood lead exposure," "pediatric blood lead levels," "childhood Pb," or "cord blood lead." Key words used to capture the outcome of interest included "cognitive," "IQ," "neurological," "intellectual function," "brain," "mental health," or "criminal." Further, in order to capture longitudinal studies, or studies that followed their cohort into adulthood, additional key words included "longitudinal," "prospective," "retrospective," "adult," "adulthood," or "adults."

Inclusion criteria included reported childhood lead exposure measured via blood lead levels with a central tendency metric of 10 µg/dL or less and longitudinal studies that measured blood lead levels in children and followed those children to measure health outcomes in the same cohort as adults. Exclusion criteria included cross-sectional studies, longitudinal studies of occupational cohorts, short-term follow-ups from geographical areas with large amounts of lead contamination (e.g. smelter communities), and lead exposure measured via bone lead.

It is important to note the differences in the evidence between cross-sectional and longitudinal studies. Correlation does not equal causation. This mantra of epidemiology helps to classify the difference between cross-sectional and prospective cohort studies. Cross-sectional studies measure exposure and outcome at the same point in time. These studies can be informative, especially when investigating a newly hypothesized association between an exposure and a

health outcome (Caruana et al. 2015). However, they are not designed to answer questions of causation. Primarily because temporality, one of the Bradford Hill Criteria, is necessary to establish causation from observational studies.

In a cross-sectional study, there is no way to ascertain if the exposure was experienced before the health outcome developed (Boyko 2013). Statistically significant results of a cross-sectional study indicate a correlation between the studied exposure and outcome. Conversely, prospective cohort studies measure exposure repeatedly over time, and before the detection or measurement of the desired outcome.

There may be other sources of bias in a particular prospective cohort study, but temporality concerns have largely been addressed through the study design. Therefore, prospective cohort studies are preferred as these studies can be used for establishing a causational relationship between an exposure and health outcome.

Results of the Literature Review

All studies were reviewed for applicability that were found in either of the two summary tables in the Toxicological Profile for Lead (ATSDR 2020) - Table 2-29: Overview of Neurological Effects in Adults Associated with Chronic Exposure to Lead and Table 2-32: Summary of Epidemiology Studies Evaluating Neurodevelopmental Effects in Adults at Mean Blood lead Concentration ≤ 10 µg/dL – or the table contained in Appendix A of the National Toxicology Program (NTP) Monograph (NTP 2012a) - Human Studies of Neurological Effects of Lead Considered in Developing Conclusions. Additionally, any non-occupational studies reported in the Shih et al. (2007) review were considered.

The papers found in these three sources as well as those from the independent literature review were not appropriate, as they either represented cross-sectional associations, represented higher blood lead populations, or were not evaluating the effects of blood lead measured during childhood on health outcomes assessed as adults.

Excluded Studies

The Cincinnati Lead Study cohort was part of several longitudinal evaluations of potential risk factors associated with cognition (Brubaker et al. 2010; Cecil et al. 2008; Cecil et al. 2011; Yuan et al. 2006). One study used this cohort to evaluate associations between BLL and criminal arrests (Wright et al. 2008). However, it was noted by authors that over 99% of this cohort had measured BLL levels above 10 µg/dL before the age of 5 Cecil et al. (2008; 2011). Due to high BLL exposures, these studies were not reviewed.

Two longitudinal studies considered members of the Boston cohort to evaluate IQ and risk factors for Alzheimers disease (Mazumdar et al. 2011; Mazumdar et al. 2012). However, the authors noted that only five participants had blood lead concentrations that never exceeded 10.0 µg/dL at any time point. The lead exposure to these children was too high to be considered for this review.

McFarlane et al. (2013) analyzed a subset of the Port Pirie, Australia cohort to evaluate an association between childhood lead exposure and adult mental health problems, which included both childhood lead concentrations and adult mental health data for 210 participants. The participants had a mean blood lead level concentration (calculated as an area under the curve) of 17.2 µg/dL from birth through 7 years of age. Capillary blood lead samples were collected at 6, 15, and 24 months and then annually until the child reached age 7. The lead exposure to these children was too high to be considered for this review.

The Dunedin Multidisciplinary Health and Development Study included individuals who were born between April of 1972 and March of 1973 at Queen Mary Maternity Hospital in Dunedin, New Zealand. The majority of this cohort population self-identified as white (> 93%). Blood lead measurements were collected for 925 participants at 11 years of age. Reuben et al. (2017) measured cognitive function at 38 years of age using the Wechsler Adult Intelligence Scale-IV, which generates the overall full-scale IQ, verbal comprehension, perceptual reasoning, working memory, and processing speed in a population from the Dunedin, New Zealand cohort. Childhood blood lead levels (collected at age 11) for 565 participants of this study were found to range from 4 to 31 µg/dL [mean (SD) = 10.99 (4.63) µg/dL]. The central tendency for this study exceeded the 10 µg/dL. Furthermore, several analyses were conducted that used those with exposures < 5 µg/dL as the referent group. Therefore, the findings from these studies cannot be generalized to the Flint children.

Beckley et al. (2018) used the same New Zealand Cohort to evaluate associations between BLL and criminal status. Reuben et al. (2019) also used this cohort to evaluate associations between childhood BLL exposure and personality, psychopathology and mental disorder symptoms in adulthood. Due to the high lead exposures, these studies did not meet the inclusion criteria for this review.

Opler et al. (2008) combined the population from their 2004 study with a similar population to increase their ability to detect a statistically significant association between blood lead and schizophrenia. However, the cut point for comparison of BLL and the odds schizophrenia was 15 µg/dL. This means that the control group had BLL below 15 µg/dL, which is higher than the central tendency of interest for this review.

Based on the literature search described above, there is no scientific evidence available to draw conclusions regarding long term cognitive effects in adulthood due to low childhood exposures. No paper met the inclusion criteria of having a central tendency BLL less than 10 µg/dL.

2.8 THERE IS NO SCIENTIFIC EVIDENCE THAT LOW BLOOD LEAD LEVELS (MEASURED AS ≤ 5 µg/dL) ARE ASSOCIATED WITH CRIMINALITY OR DELINQUENCY

I conducted a literature search using PubMed using the following search terms: ((blood lead [mesh]) AND (arrests OR criminality OR crime OR criminal behavior OR delinquency OR delinquent OR juvenile delinquency)). 50 studies were identified as a result of this search. I then reviewed the papers for the following inclusion criteria: having blood lead measures and quantifiable metrics for criminal acts (e.g. homicide, arrests). Ecological studies were excluded from the evaluation. Four studies remained from the original search, one additional study was identified by screening the review papers identified in the original search, and one study was identified from the NTP 2012 report (Beckley et al. 2018; Emer et al. 2020; Hornung et al. 2009; Lob and Desbaumes 1976; Sampson and Winter 2018; Wright et al. 2008).

Of the identified studies, none of the studies reflected low blood lead levels of exposure. The lowest observed central tendency of blood lead levels was identified in a Chicago 18 year follow-up birth cohort with a mean blood lead level of 6.2 µg/dL which was collected on participants by age 6 years (Sampson and Winter 2018). Arrest records provided by the Illinois Criminal Justice Information Authority were reviewed. Authors noted that even though individuals who had been arrested had slightly higher blood lead levels (6.55 µg/dL) than those who were never arrested (6.10 µg/dL), the association between blood lead level and arrests was not statistically significant.

These findings remained even after adjustment for gender, race/ethnicity, immigrant generation, primary caregiver education level, neighborhood socioeconomic status, and neighborhood racial composition (Sampson and Winter 2018).

Two studies evaluated the Cincinnati Lead Study cohort and did observe significant associations between blood lead levels and arrests (Hornung et al. 2009; Wright et al. 2008). Wright et al. (2008) evaluated prenatal blood lead levels via maternal measurements in the first or early second trimester of pregnancy, early childhood average blood lead levels (defined as the average of 23 blood lead concentrations obtained quarterly from age 3 to 60 months and semiannually from 66 to 78 months), and six-year blood lead concentrations with violent crime arrests. The rate ratio of violent crime arrests for each 5 µg/dL increase in BLL was significant for childhood average BLL (median 12.3 µg/dL; RR = 1.30; 95% CI: 1.03-1.64) and for six-year average (median 6.8 µg/dL; RR = 1.48; 95% CI: 1.15-1.89) but not for prenatal blood lead levels. Hornung et al. (2009) combined data from the Cincinnati Lead Study with the Rochester Longitudinal cohort. The peak BLL of the combined group of children with 13.6 µg/dL with early childhood BLL of 8.9 µg/dL and concurrent BLL of 6.0 µg/dL. Similar findings were observed in this analysis as those reported in Wright et al. (2008).

Emer et al. (2020) conducted a historical cohort study of Milwaukee residents. Blood lead measures collected between June 1, 1986 and December 31, 2003, by age six years, and reported to the Milwaukee Health Department were linked to firearm violence perpetration that occurred between January 1st, 2005 and December 31st, 2015. Logistic regression was used to estimate odds of firearm violence due to BLL with models being adjusted for child sex, race, socioeconomic status, and year of birth. The reference group included all children with mean or peak BLL < 5 µg/dL. For the fully adjusted models, there was statistically significant increased odds of firearm violence for all comparison groups relative to those with BLL < 5 ug/dL. An evaluation of continuous BLL demonstrated that for every 1 ug/dL increase in mean childhood BLL, the odds of firearm violence increased 3% (95% CI: 1 – 4%).

Beckley et al. (2018) conducted a population-based prospective cohort study of individuals born between April 1, 1972 and March 31, 1973. The participants were part of the Dunedin Multidisciplinary Health and Development Study in New Zealand. Observations of potential violent crimes, nonviolent crimes, and recidivism were conducted in December 2012, when participants were 38 years of age. Blood lead levels were collected at 11 years of age and the mean BLL was 11.01 ug/dL. Conviction records were obtained from the New Zealand police department. Logistic regression analyses were only adjusted for sex. The odds of criminal conviction was not statistically associated with BLL (OR = 1.23; 95% CI: 1.00 – 1.51) nor was the odds of being a violent offender (OR = 1.13; 95% CI: 0.82 – 1.55). However, the odds of being a nonviolent offender was borderline significant (OR = 1.28; 95% CI: 1.01 – 1.61).

The oldest study comparing BLL and crime was conducted in the early 1970s in Switzerland where BLL were compared between prisoners and a comparison population living in Lausanne. The blood lead levels between the two groups were not statistically different and the BLL measures exceeded 20 ug/dL (Lob and Desbaumes 1976).

None of these studies reflect the level of lead exposure observed in Flint. Additionally, the findings across studies are inconsistent and not all studies adjusted for relevant confounding factors. There are no studies that provide evidence of criminality at blood lead levels under 5 µg/dL.

Due to the paucity of data on criminality, some research groups combine criminality with conduct disorder or behavioral evaluations. The NTP 2012 report concluded that “[t]here is inadequate evidence to evaluate the potential association between blood Pb <10 µg/dL and effects on

behavior problems in adults" (NTP 2012b, p. 35). However, the EPA concluded "Pb-associated increases in conduct disorders were found in populations with mean blood Pb levels 7-14 µg/dL. Associations with lower blood Pb levels that are not influenced by higher earlier Pb exposures are not well characterized" (EPA 2013, p. 1-22). These observations are similar to those reported in the most recent ATSDR evaluation of lead where "[a]ltered mood and behaviors that may contribute to learning deficits, including attention deficits, hyperactivity, autistic behaviors, conduct disorders, and delinquency" have been observed at BLL ≤ 10 µg/dL (ATSDR 2020, p. 133).

Based on the literature search described above, there is no scientific evidence available to draw conclusions regarding the association between criminality and delinquency due to low childhood exposures (BLL ≤ 5 µg/dL).

2.9 CONTRARY TO THE OPINIONS EXPRESSED BY DR. HOWARD HU THERE IS INSUFFICIENT SCIENTIFIC EVIDENCE TO DRAW A CAUSAL CONNECTION BETWEEN LOW LEVEL LEAD EXPOSURE (< 5 µg/dL) AND IQ DECREMENTS IN CHILDREN.

Dr. Howard Hu opined in his declaration that the magnitude and duration of lead exposure was sufficient so that "each child [in Flint] will have sustained non-negligible impairment of their neurobehavioral development" (Hu Declaration Dated June 29, 2020: p. 9-10) and he also provided citations for "individual analyses, meta-analyses, and reviews" that he believes support his opinion (Hu Declaration Dated June 29, 2020: p. 27-28). He further stated that because the "magnitude of lead exposure and resulting impact on IQ is modest, such pre- and post-testing may not be able to reliability distinguish 'true' changes in IQ from the random 'noise' that typically occurs when IQ tests are repeated in the same individual" (Hu Declaration Dated June 29, 2020: p. 33). Dr. Hu agreed that there are chemicals other than lead that can effect IQ including PCBs, mercury, PBDEs and fluoride (Remote Video Taped Deposition of Howard Hu, MD, Dated October 12, 2020: p. 194-195). He also conceded that the home environment and parental IQ are important factors associated with a child's IQ development (Remote Video Taped Deposition of Howard Hu, MD, Dated October 12, 2020: p. 197).

During his deposition however, Dr. Hu restricted his opinion to low level lead exposure as a cause of IQ decrements in children and not any other neurobehavioral impairments. (Remote Video Taped Deposition of Howard Hu, MD, Dated October 12, 2020: p. 194).

In my opinion, the scientific literature relied upon by Dr. Hu does not support his opinion that there is a causal connection between low level lead exposure in children and IQ decrements. All class representative BLL as reported in this case are low (< 5 µg/dL). There is insufficient scientific evidence to support such a conclusion for the following reasons.

The literature cited by Dr. Hu includes Scwhartz (1994) and the Lanphear et al. (2005) international pooled analysis.. He also cites a re-analyses of the Lanphear et al. Lanphear et al. (2005) international pooled cohort conducted by Budtz-Jørgensen et al. (2013). He includes the work of Jakubowski et al. (2011) and Carlisle et al. (2009) who conducted analyses using the original Lanphear et al. (2005) data. However, Dr. Hu omits the re-evaluation of the international pooled analysis conducted by Crump et al. (2013) While it is true that a harmful threshold of lead exposure has not have been identified, as described in previous sections of my report, the Crump et al. (2013) analysis demonstrates that the statistical power at low BLL exposures is too low to draw conclusions regarding associations between low BLL with IQ, especially for concurrent BLL

< 5 ug/dL and peak BLL < 7 µg/dL. In fact, the Lanphear et al. (2005) data included children where over 92% had peak blood lead levels that exceeded 7.5 µg/dL.

In addition to demonstrating low statistical power, Crump et al. (2013) confirmed original analyses conducted by Lanphear et al. (2005). Lanphear et al. (2005) defined four BLL metrics: concurrent, early, lifetime and peak. Concurrent BLL reflects the BLL measured closest to the IQ test. Early BLL was defined as the mean BLL from 6 months to 24 months. Lifetime BLL was defined as the mean BLL from 6 months to the concurrent BLL test. Peak BLL is the maximum BLL measured at any time prior to the IQ test. Lanphear et al. (2005) then separated the data by levels of exposure and conducted analyses at two different cut points, 7.5 µg/dL and 10 µg/dL. This allows for the evaluation of the association between low BLL and IQ because analyses excluded children with exposures above those cut points.

The only metric that was statistically significant at low BLL exposures as defined by Lanphear et al. (2005) was observed for concurrent BLL in children with BLL < 7.5 µg/dL but this relationship did not hold for all children with concurrent exposures < 10 µg/dL. There was no statistically significant association between low BLL and IQ for peak, early or lifetime average BLL < 7.5 or < 10 µg/dL. As stated by Crump et al. (2013), "[t]aken at face value, use of concurrent BPb to describe the exposure response implies that the effect of BPb upon IQ is reversible, as zero concurrent BPb would indicate zero effect of BPb upon IQ, regardless of the past history of exposure" (p. 797).

Two newer studies, described in detail above, show that there was no association between low prenatal and/or concurrent blood lead levels < 5 µg/dL and IQ (Desrochers-Couture et al. 2018; Taylor et al. 2017). Dr. Hu cites both of these publications in his report, but fails to provide the reader with details regarding the statistical significance, or lack thereof as reported by the authors. In summarizing Taylor et al. (2017) Dr. Hu wrote "and another showing weak (in boys) or no (in girls) adverse impacts of prenatal blood lead levels on the IQ of children at 4 and 8 years of age among mothers with a median blood lead level during pregnancy of 3.7 µg/dL" (Hu Declaration Dated June 29, 2020: p. 41). The findings in Taylor actually reported statistically significant positive associations with BLL and IQ in girls. This means that for increasing BLL there was observed a statistically significant increase in IQ in the regression analysis. However, for boys, there was no statistically significant association between BLL and IQ ($p > 0.1$). In describing the Desrochers-Couture et al. (2018) study Dr. Hu wrote "among children whose mothers during pregnancy had blood lead levels ranging from 0.14 to 4.14 µg/dL showing a profound effect on boys (with a 1 µg/dL increase in umbilical cord blood lead associated with a 2.65 point decline in IQ) but not on girls" (Hu Declaration Dated June 29, 2020: p. 40). However, this is not the conclusion of the authors. As reported in the publication "[n]o associations were found between WPPSI-III [IQ] scores and prenatal maternal blood or concurrent child blood lead concentrations" (Desrochers-Couture et al. 2018; p. 120).

Therefore, in my opinion, the lack of statistically significant associations for low exposures for a majority of exposure metrics as defined by Lanphear et al. (2005), the conflicting results for children with concurrent BLL < 7.5 µg/dL and for children with concurrent BLL < 10 µg/dL, and newer longitudinal studies failing to observe associations between low BLL and IQ demonstrates the scientific data at low BLL does not support causal connection between the impact of such exposures on IQ.

3 CLOSING STATEMENT

I submit these opinions to a reasonable degree of scientific certainty and am prepared to support them in both deposition and/or courtroom testimony. I may supplement this report if additional information becomes available or I am asked to address other issues.

Respectfully,

January 4, 2021

Stacey M. Benson, PhD
Senior Managing Health Scientist

Date

APPENDIX

A

Curriculum Vitae

Stacey M Benson, PhD

Current Position
Senior Managing Health Scientist

Discipline Areas
> Epidemiology
> Occupational and Health Safety Sciences

Years' Experience
16

Joined Cardno
2014

Education
> PhD, Epidemiology, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, 2011 – 2014
> MS, Exercise Physiology, University of Pittsburgh, School of Education, Pittsburgh, PA, 2005 - 2007
> BS, Physics, St. Lawrence University, Canton, New York, 1996-2000

Summary of Experience

Dr. Stacey M. Benson is a Senior Managing Health Scientist with Cardno ChemRisk in the Pittsburgh, PA office. She received her undergraduate training in physics from St. Lawrence University, completed a Master's of Exercise Physiology from the University of Pittsburgh in 2005, and completed her doctorate in Environmental Epidemiology from the University of Pittsburgh in 2014. The focus of her dissertation was to assess the relationship between industrial and aviation ambient air lead emissions and blood lead levels in children between 0 and 5 years of age. Prior to joining Cardno ChemRisk, Dr. Benson worked as an Associate Service Fellow for the National Institute of Occupational Safety and Health, National Personal Protective Technology Laboratory. During her work with NIOSH, she applied skills in technical writing and editing, data analysis, and 3-D anthropometric computer modeling in an effort to improve respirator headform designs for civilian workers in the U.S. and China. In addition, Dr. Benson's role also included recruiting hundreds of participants for participation in several human subject research studies, drafting research proposals and IRBs, working with participants to ensure understanding of their voluntary involvement in their respective study according to IRB regulations, coordinating participant schedules, addressing participant questions and concerns, and collecting physiological and anthropometric data from the participants.

Significant Projects

Regulatory Work

Pre-Market Tobacco Applications

Dr. Benson is responsible for leading the clinical team to support PMTA submissions. She is responsible for clinical study design and research strategies for human subject research that informs on the health effects of new tobacco products (e.g. electronic nicotine delivery systems, oral nicotine products). These submissions are complex and require systematic literature reviews, pharmacokinetic studies, behavioral surveys, biomonitoring studies, and population modeling to evaluate the overall impact of new tobacco products on population health. Clients also need to test their products for harmful or potentially harmful constituents, conduct leachable and extrable studies,and toxocilogical evaluations of their products. Dr. Benson works closely with the non-clinical team who provide support on chemistry and toxicology testing for our PMTA clients. As a research group, we provide clinical and non-clinical study oversight, we synthesize reseach findings, draft briefing packages, and draft full PMTA submissions.

Occupational Safety and Health

Laboratory Study to Assess Causative Factors Affecting Temporal Changes in Filtering-Facepiece Respirator Fit (2009-2011)

Dr. Benson's role included recruiting over 200 participants for a multi-visit 3-year study. She ensured that each participant met specific study criteria, worked with participants to ensure understanding of their voluntary involvement in the study according to IRB regulations, coordinated participant schedules for their bi-annual visits and addressed participants questions and concerns. She collected several types of data: physiological, anthropometric facial measurements, 3-D scans using 3dMD technology and fit tests.

She was responsible for data analysis and technical writing acting as a co-author on several publications and presentations for national and international conferences.

NIOSH Anthropometric Studies to Develop Headforms for U.S. and Chinese Civilian Populations (2007 – 2010)

Dr. Benson was responsible for developing headforms that adequately represent the U.S. workforce. In 2003, NIOSH conducted an anthropometric survey of 3,997 subjects and collected data on 26 landmark locations. A subset of the sample (n = 973) were scanned with a Cyberware 3-D Rapid Digitizer. As a certified Polyworks user, she developed modeling techniques that converted scans of 5 subjects whose facial measurements most closely matched criteria indicating a specific head size into a single representative headform. Five unique sizes were constructed: small, medium, large long/narrow and short/wide. Since their development these headforms have been incorporated into a technical specification standard for ISO TC94 Personal Protective Equipment, SC15 Respiratory Protective Devices, WG1 General, PG5 Human Factors. That standard is titled “ISO 16976-2 Respiratory Protective Devices — Human Factors — Part 2: Anthropometrics”. This methodology was then used to construct 5 representative headforms for Chinese civilian workers based on an anthropometric survey of 3000 Chinese civilian workers of whom 350 received scans.

Environmental Sampling

Conducted area sampling on a hydraulic fracturing site to collect background data on total VOCs, 75 individual VOCs, hydrogen sulfide, nitrogen oxides, carbon monoxide, PM2.5, PM10 and ambient noise.

Conducted personal air and area dust sampling to evaluate potential crystalline silica and mineral wool fiber exposures of commercial ceiling installers during simulated ceiling tile installation and removal.

Conducted area sampling for VOCs, SVOCs, sulfur compounds, amines, nitrosamines, and general air quality in a residential setting with alleged paint off-gases.

Litigation Support

As project manager, directed project staff to review and summarize case materials, including deposition transcripts and MSDSs.

Prepared case summaries, expert reports, and affidavits for toxic tort litigation cases involving occupational exposures to asbestos fibers, diesel, fiberglass, benzene, and formaldehyde.

Conducted literature reviews to provide litigation support on cases with alleged exposure to asbestos, benzene, diesel, fiberglass, and other chemical agents.

Statistical Analysis

Used survey weighted analytical techniques to evaluate nicotine containing product use from nationally representative surveys conducted in the US (e.g. NHANES, PATH, and NYTS).

Performed systematic review and meta-analysis of occupational exposure to diesel exhaust in the railroad industry and the risk of lung cancer.

Used indirect adjustment techniques to evaluate the influence of smoking on lung cancer risk estimates for occupational exposure studies that could not account for such behavior due to a lack of smoking data for individuals included in the original studies.

Conducted quasi-experimental design using logistic and Poisson regression techniques to determine if a chemical spill affected the prevalence of adverse birth outcomes in the potentially exposed population.

Performed a systematic review and meta-analyses of occupational exposure to asbestos and the risk of laryngeal and pharyngeal cancer by fiber type.

Used NHANES data and survey weighted regression analyses to evaluate environmental exposures and childhood blood lead levels.

Membership and Service to Professional Societies

- American Thoracic Society (ATS), 2015 – Current
- International Council on Surgical Plume, Inc. (ICSP), 2015 – Current
  - Inaugural member of the Clinical Advisory Committee
- International Society of Environmental Epidemiology (ISEE), 2012 – 2013

Publications

Peer-Reviewed Publications

- Egnot, N.S., S.M. Benson, M.F. Vater, R. Hazan, O. Patel, and G.M. Marsh. 2020. Systematic review and meta-analysis of epidemiological literature evaluating the association between exposure to man-made vitreous fibers and respiratory tract cancers. Reg Tox Pharm. Advance online publication, Jan. 25, 2020. doi: 10.1016/j.yrtph.2020.104585.
- Marsh, G.M., A.M. Ierardi, S.M. Benson, and B.L. Finley. 2019. Response to letters regarding “Occupational exposures to cosmetic talc and risk of mesothelioma: an updated pooled cohort and statistical power analysis with consideration of latency period.” Inhal Tox. Advance online publication, Dec. 18, 2019. doi: 10.1080/08958378.2019.1702744.
- Benson, S.M., J.R. Maskrey, M.D. Nembhard, K.M. Unice, M.A. Shirley, and J.M. Panko. 2019. Evaluation of personal exposure to surgical smoke generated from electrocautery instruments: A pilot study. Ann Work Exp Health. Advance online publication, Oct. 3, 2019. doi: 10.1093/annweh/wxz070.
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- Marsh, G.M., K.A. Keeton, A.S. Riordan, E.A. Best, and S.M. Benson. 2019. Ethylene oxide and risk of lympho-hematopoietic cancer and breast cancer: A systematic literature review and meta-analysis. Int Arch Occup Env Health. Advance online publication, May 20, 2019. doi: 10.1007/s00420-019-01438-z.
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> Marsh, G.M., A.S. Riordan, K.A. Keeton, and S.M. Benson. 2018. Response to: 'Reanalysis of non-occupational exposure to asbestos and the risk of pleural mesothelioma' by Finkelstein. Occup Env Med. Advance online publication, March 24, 2018. doi: 10.1136/oemed-2018-105020.

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> Marsh, G.M., A.S. Riordan, K.A. Keeton, and S.M. Benson. 2017. Non-occupational exposure to asbestos and risk of pleural mesothelioma: Review and meta-analysis. Occup Env Med. 74:838-846.

> Finley, B.L, S.M. Benson, and G.M. Marsh. 2017. Cosmetic talc as a risk factor for pleural mesothelioma: A weight of evidence evaluation of the epidemiology. Inhal Tox. 29(4):179-185.

> Benson, S.M., P. Ruestow, K.A. Keeton, R.M. Novick, G.M. Marsh, and D.J. Paustenbach. 2017. The 2014 crude 4-methylcyclohexanemethanol chemical release and birth outcomes in West Virginia. Arch Env Occup Health. Advance online publication, July 10, 2017. doi: 10.1080/19338244.2017.1350132.

> Cowan, D.M., S. Benson, T.J. Cheng, S. Hecht, N.M. Boulos, and J. Henshaw. 2017. Evaluation of reported fatality data associated with workers using respiratory protection in the United States (1990-2012). Arch Env Occup Health. 72(4):235-246.

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> Brink LL, SM Benson, LP Marshall and EO Talbott. 2014. Environmental Inequality, adverse birth outcomes, and exposure to ambient air pollution in Allegheny County, PA, USA. J Racial and Ethnic Health Disparities: 1-6.

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Presentations

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> Egnot, N.S., S.M. Benson, M.F. Vater, R. Hazan, O. Patel, A. Bowman, G.M. Marsh. 2019. Systematic Review and Meta-Analysis of Epidemiological Literature Evaluating the Association Between Exposure to Man-Made Vitreous Fibers and Respiratory System Cancers. Poster Presentation at the 2019 Society of Toxicology Conference (SOT) Annual Meeting, March 10-14, Baltimore, MD.

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> Keeton, KA, SM Benson, RM Novick, GM Marsh and DJ Paustenbach. 2017. The 2014 Crude 4-Methylcyclohexanemethanol Chemical Release and Birth Outcomes in West Virginia. Poster presentation at Society of Epidemiologic Research. June 20-23, 2017, Seattle, WA.

> Benson, S.M., G.M. Marsh and B.L. Finley. 2017. Cosmetic Talc as a Risk Factor for Mesothelioma: A Weight-of-Evidence Evaluation. Abstract #1290. Poster Presentation at Society of Toxicology Annual Meeting. March 12-16, 2017. Baltimore, Maryland.

> Burns, A.M., S.M. Benson. 2017. Emerging Litigations: Cosmetic Talc and Hydraulic Fracturing. Session 1: State of Science in Cosmetic Talc Litigation. Continuing Legal Education (CLE) Seminar provided by Dickie, McCamey & Chilcote, P.C. August 23, 2017, Pittsburgh, PA.

> Benson, SM, S Batdorf, KM Hitchcock, DA Galbraith and BL Finley. 2016. Asbestos exposure and pharyngeal and laryngeal cancer risk: A fiber-type specific meta-analysis. Abstract #2974. Poster Presentation at Society of Toxicology Annual Meeting. March 13-17, 2016. New Orleans, Louisiana.

> Panko, JM, SM Benson and ML Kreider. 2016. Meta-analysis of lung cancer risk related to diesel exposure by occupation and evaluation of exposure response.

Abstract #2976. Poster Presentation at Society of Toxicology Annual Meeting. March 13-17, 2016. New Orleans, Louisiana.

> Benson SM, P Ruestow, T Duke and PK Scott. 2015. "Influence of asthma, smoking, and obesity on lung function parameters in the US adult population: NHANES 2007-2012." Poster at the annual American Thoracic Society conference.

> Brink L, L Marshall, SM Benson and E Talbott. 2013. "Adverse Birth Outcomes Associated with Exposure to Ambient Air Pollution in Allegheny County, PA, US" Poster at the annual International Society for Environmental Epidemiology conference.

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> Benson S, R Sharma and E Talbott. 2012. "Estimated Risk of Fatal Cancer due to the Nuclear Emergency at the Fukushima Daiichi Plant" Poster at the annual International Society for Environmental Epidemiology conference.

> Benson S, T Rozzi, J Snyder, and D Novak. 2011. "Aromatic Hydrocarbon Adsorption Characteristics of Disposable Filtering Facepiece Respirators that Contain Activated Charcoal. Poster at the National Institute of Occupational Safety and Health, Personal Protective Technology Stakeholders Meeting.

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> Zhuang Z, A Palmiero, SM Benson, M Bergman, R Roberge and J Williams. 2011. Laboratory Study to Assess Causative Factors Affecting Temporal Changes in Filtering-Facepiece Respirator Fit: Part II – One Year Assessment of Fit Changes" Poster at the National Institute of Occupational Safety and Health, Personal Protective Technology Stakeholders Meeting.

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> Benson SM, W Chen, J Hsiao, D Yu, H Wang and Z Zhuang. 2010. Digital 3-D headforms representative of the current Chinese workers. Poster at American Industrial Hygiene Conference & Exposition

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- Chen W, Z Zhuang, SM Benson, L Du, D Yu, D Landsittel, et al. 2008. “New Respiratory Fit Test Panels Representing the Current Chinese Civilian Workers” Presentation at International Society of Respiratory Protection.
- Zhuang Z,D Groce, HW Ahlers, W Iskander, D Landsittel, S Guffey, et al. 2008. “Correlation between Respiratory fit and respirator fit test panel cells by respirator size”. Presentation at International Society of Respiratory Protection.

APPENDIX

B

Materials Reviewed and References

Materials Reviewed and References

MATERIALS REVIEWED IN FORMULATING OPINIONS

My opinions are provided in Section 2 of this report. These opinions are based on my professional qualifications, work experiences, and knowledge of industrial hygiene, toxicology, health risk assessment, and related fields. My opinions also are based on information that is related to this case. In the process of preparing this report, I have reviewed and relied upon the following case-specific documents:

Darnella Gaines

1. Veolia Water North America Operating Services, LLC's Veolia North America, LLC's, and Veolia North America, Inc.'s First Set of Interrogatories to the Plaintiff Darnella Gaines as she is next Friend of the Minor Plaintiff K.C. (dated August 18, 2020)
2. Veolia Water North America Operating Services, LLC's Veolia North America, LLC's, and Veolia North America, Inc.'s First Request for Production of Documents and Tangible Things by the Plaintiff Darnella Gaines, in her Capacity as next Friend of the Minor Plaintiff K.C. (dated August 19, 2020)
3. Confidentiality Addendum to Plaintiff Darnella Gaines', as the Next Friend of K.C., a Minor, Response to VNA Defendants' First Set of Interrogatories To K.C., a Minor (dated September 9, 2020)
4. Plaintiff Darnella Gaines, as the next Friend of Plaintiff K.C., a Minor, Response to VNA Defendants' First Set of Interrogatories (dated September 9, 2020)
5. Plaintiff Darnella Gaines, as the next Friend of Plaintiff K.C., a Minor, Response to VNA Defendants' First Request for Production of Documents and Tangible Things (dated September 10, 2020)
6. Deposition Transcript of Darnella Gaines (dated September 14, 2020)
7. Blood Lead Test Requisition for Minor, K.C. (dated July 25, 2012)
8. [redacted] Blood Lead Levels for Minor,. KC (dated March 23, 2017)
9. [redacted] Blood Lead Levels for Minor,. KC (dated May 13, 2017)
10. Various Education Records (various dates)
11. Various Medical Records (various dates)

[redacted]

1. [redacted] Bone Lead Scan Results (specimen date August 11, 2004)
2. [redacted] Bone Lead Scan Results specimen (specimen date September 21, 2015)
3. [redacted] Bone Lead Scan Results specimen (specimen date November 5, 2015)
4. [redacted] Bone Lead Scan Results specimen (specimen date November 5, 2015)
5. Various Authorization Forms (various dates)
6. Various Education Records (various dates)
7. Various Medical Records (various dates)
8. Various [redacted] (various dates)

Appendix B

Rhonda Kelso

1. Deposition Transcript of Rhonda Kelso (dated November 12, 2019)
2. Continued Deposition Transcript of Rhonda Kelso (dated November 12, 2019)
    a. Exhibit 1 – Fourth Consolidated Amended Class Complaint for Injunctive and Declaration Relief, Money Damages and Jury Demand (dated October 5, 2018)
    b. Exhibit 2 – Plaintiff Rhonda Kelso's, as Next Friend of K.E.K., a Minor Child, Response to Defendants' First Set of "Uniform" Interrogatories (dated June 6, 2019)
    c. Exhibit 3 – Plaintiff Rhonda Kelso's, Response to Defendants' First Set of "Uniform" Interrogatories (dated June 6, 2019)
    d. Exhibit 4 – ATC Report 'Lead-Based Paint Inspection/Risk Assessment Report for Property Located at [redacted] (dated August 29, 2018)
    e. Exhibit 5 – [redacted] (dated September 30, 2015)
    f. Exhibit 6 – [redacted] – Report of Blood Lead Specimen Results (specimen date August 11, 2004)
    g. Exhibit 7 – [redacted] – Report of Blood Lead Specimen Results (specimen date September 21, 2015)
    h. Exhibit 8 – Medical Records of K.E.K., a Minor Child from [redacted] (service date November 5, 2015)
    i. Exhibit 9 – Medical Records of K.E.K., a Minor Child from [redacted](service date November 5, 2015)
    j. Exhibit 10 – [redacted] – Report of Blood Lead Specimen Results (specimen date November 5, 2015)
    k. Exhibit 11 – Records of K.E.K., a Minor Child from [redacted] (dated August 1, 2003)
    l. Exhibit 12 – Tap Water Lead Sample Results from Virginia Tech (dated December 8, 2015)
    m. Exhibit 13 – Water Test Results from Michigan Department of Environmental Quality (date tested December 15, 2015)
    n. Exhibit 14 – Comment from Rhonda Kelso (dated October 15, 2015)
    o. Exhibit 15 – Comment from Rhonda Kelso (dated September 29, 2015)
    p. Exhibit 16 – Sample Results Report from ALS Environmental (dated September 20, 2016)
    q. Exhibit 17 – Sample Results Report from ALS Environmental (dated May 2, 2017)
    r. Exhibit 18 – Medical Records of K.E.K., a Minor Child from [redacted] (dated November 10, 2016)
    s. Exhibit 19 – Medical Records of K.E.K., a Minor Child from [redacted] Communication (dated February 4, 2016)

t. Exhibit 20 – Confidential Addendum to Plaintiff Rhonda Kelso's Amended Response to Defendants' First Set of "Uniform" Interrogatories (dated July 8, 2019)

3. Plaintiff Rhonda Kelso's, as Next Friend of K.E.K., a Minor Child, Response to Defendants' First Set of "Uniform" Interrogatories (dated June 6, 2019)
4. Plaintiff Rhonda Kelso's, Response to Defendants' First Set of "Uniform" Interrogatories (dated June 6, 2019)
5. Plaintiff Rhonda Kelso's, both Individually and as Next Friend of the Minor K.E.K., Response to Defendants Veolia Water North America Operating Services, LLC's Veolia North America, LLC's and Veolia North America, Inc.'s Second Request for Production of Documents and Tangible Things (June 6, 2019)
6. Plaintiff Rhonda Kelso's, both Individually and in her Capacity as Next Friend of the Minor K.E.K., Response to Defendants Lockwood, Andrews and Newman, Inc.'s and Lockwood, Andrewes and Newman, PC's, Request for Production of Documents and Tangible Things (June 6, 2019)
7. Plaintiff Rhonda Kelos's Amended Response to Defendants' First Set of "Uniform" Interrogatories (dated July 8, 2019)
8. Confidential Addendum to Plaintiff Rhonda Kelos's Amended Response to Defendants' First Set of "Uniform" Interrogatories (dated July 8, 2019)
9. Plaintiff Rhonda Kelso's Amended Response to Defendants First Set of "Uniform" Interrogatories (July 8, 2019)
10. Plaintiff Rhonda Kelso's, as Next Friend of the K.E.K., a Minor Child, Amended Response to Defendants First Set of "Uniform" Interrogatories (July 8, 2019)
11. Plaintiff Rhonda Kelso's Amended Response to Defendants First Set of "Uniform" Interrogatories (dated July 10, 2019)
12. Plaintiff Rhonda Kelso's, as Next Friend of the K.E.K., a Minor Child, Amended Response to Defendants First Set of "Uniform" Interrogatories (July 10, 2019)
13. Confidential Addendum to Plaintiff Rhonda Kelos's Amended Response to Defendants' First Set of "Uniform" Interrogatories (dated July 10, 2019)
14. Confidential Addendum to Plaintiff Rhonda Kelos's, as Next Friend of K.E.K., a Minor Child, Amended Response to Defendants' First Set of "Uniform" Interrogatories (dated July 10, 2019)
15. Charles Stewart Mott Community College Education Records for Rhonda Kelso (dated July 3, 2019)
16. Various Medical Records (various dates)
17. Piping Information - Service Line Replacements & Copper Identification: Phase 4 (dated May 1, 2017 thru May 14, 2018)
18. Rhonda Kelso Blood Lead Levels - [redacted] Communication (dated September 30, 2015)
19. Water Testing – [redacted] Residential Testing Report – results collected through June 30, 2016

[redacted]

1. Plaintiff Tiantha Williams, both Individually and in her Capacity as Next Friend of the Minor Plaintiff T.W., Response to Defendants Lockwood, Andrews and Newman, Inc.

and Lockwood, Andrews and Newman, PC's, Request for Production of Documents and Tangible Things (June 6, 2019)

2. Plaintiff Tiantha Williams, both Individually and as Next Friend of the Minor Plaintiff T.W., Response to Defendants Veolia Water North America Operating Services, LLC's Veolia North America, LLC's and Veolia North America, Inc.'s Second Request for Production of Documents and Tangible Things (June 6, 2019)
3. Plaintiff Tiantha Williams, as Next Friend of T.W., a Minor Child, Response to Defendants' First Set of "Uniform" Interrogatories (dated June 6, 2019)
4. Plaintiff Tiantha Williams, Response to Defendants' First Set of "Uniform" Interrogatories (dated June 6, 2019)
5. Confidentiality Addendum to Plaintiff Tiantha Williams Responses to Defendants' First Set of "Uniform" Interrogatories (dated July 1, 2019)
6. Plaintiff Tiantha Williams Response to Defendants' First Set of "Uniform" Interrogatories (dated July 1, 2019)
7. Blood Lead Level Results from [redacted] for T.W., a Minor (date reported March 2, 2017)
8. Blood Lead Level Results from [redacted] for T.W., a Minor (date reported March 21, 2017)
9. Blood Lead Level Results from [redacted] for T.W., a Minor (date reported May 18, 2016)
10. Blood Lead Level Results from [redacted] for T.W., a Minor (date reported June 26, 2017)
11. Blood Lead Level Results from [redacted] for T.W., a Minor (date reported December 21, 2016)
12. [redacted] Education Records for T.W., a Minor (dated August 20, 2019)
13. Various Medical Records (various dates)

<u>Tiantha Williams</u>

1. Blood Lead Levels - [redacted]
2. Plaintiff Tiantha Williams, both Individually and in her Capacity as Next Friend of the Minor Plaintiff T.W., Response to Defendants Lockwood, Andrews and Newman, Inc. and Lockwood, Andrews and Newman, PC's, Request for Production of Documents and Tangible Things (June 6, 2019)
3. Plaintiff Tiantha Williams, both Individually and as Next Friend of the Minor Plaintiff T.W., Response to Defendants Veolia Water North America Operating Services, LLC's Veolia North America, LLC's and Veolia North America, Inc.'s Second Request for Production of Documents and Tangible Things (June 6, 2019)
4. Plaintiff Tiantha Williams, as Next Friend to T.W., a Minor Child, Response to Defendants' First Set of "Uniform" Interrogatories (dated June 6, 2019)
5. Confidentiality Addendum to Plaintiff Tiantha Williams Responses to Defendants' First Set of "Uniform" Interrogatories (dated July 1, 2019)
6. Plaintiff Tiantha Williams Response to Defendants' First Set of "Uniform" Interrogatories (dated July 1, 2019)
7. Deposition Transcript of Tiantha Williams – Volume I (dated December 12, 2019)

a. Exhibit 1 - Confidentiality Addendum to Plaintiff Tiantha Williams Responses to Defendants' First Set of "Uniform" Interrogatories (dated July 1, 2019)
b. Exhibit 2 - Plaintiff Tiantha Williams Response to Defendants' First Set of "Uniform" Interrogatories (dated July 1, 2019)
c. Exhibit 3 – Flint Water Class Action Damage Inventory – General Instructions (no date)
d. Exhibit 4 – Medical Records of Tiantha Williams from Hamilton Community Health Network (dated July 9, 2019)
e. Exhibit 5 - Plaintiff Tiantha Williams, as Next Friend to T.W., a Minor Child, Response to Defendants' First Set of "Uniform" Interrogatories (dated June 6, 2019)
f. Exhibit 6 – Pages from Discovery Document (page 18 and 19 or 224)
a. Exhibit 7 - Blood Lead Level Results from [redacted] for T.W., a Minor (date reported March 2, 2017)
b. Exhibit 8 - Blood Lead Level Results from [redacted] for T.W., a Minor (date reported December 21, 2016)
g. Exhibit 9 - Blood Lead Level Results from [redacted] for T.W., a Minor (date reported March 21, 2017)
h. Exhibit 10 – Hydrovac door hanger from City of Flint
i. Exhibit 11 – [redacted] for Tiantha Williams (dated July 31, 2015)
j. Exhibit 12 - Blood Lead Level Results from [redacted] for T.W., a Minor (date reported March 2, 2017)
k. Exhibit 13 – Medical Records for T.W. a Minor, from [redacted] (May 23, 2016)
l. Exhibit 12 - Blood Lead Level Results from [redacted] for T.W., a Minor (date reported March 2, 2017)

8. Deposition Transcript of Tiantha Williams – Volume Ii (dated December 13, 2019)
9. Authorization to Release Records of Tiantha Williams to
   a. Jack Yates High School (dated February 27, 2019)
   b. [redacted] (dated February 27, 2019)
   c. [redacted] (dated February 27, 2019)
   d. [redacted] (dated February 27, 2019)
   e. [redacted] (dated February 27, 2019)
   f. [redacted] (dated June 28, 2019)
   g. [redacted] (dated June 28, 2019)
   h. [redacted] (dated June 28, 2019)
   i. [redacted] (dated June 28, 2019)
   j. [redacted] (dated June 28, 2019)
10. Various Medical Records (various dates)Social Security and Disability Records for Tiantha Williams (various dates)

Appendix B

Alan Ducatman

1. Deposition Transcript of Alan Ducatman, MD – Volume I (dated November 12, 2020)
2. Exhibit 120 – Declaration of Alan Ducatman, MD, MS in Support of Plaintiffs Motion for Class Certification (dated June 28, 2020)
    a. Exhibit A – Curriculum Vitae of Alan Ducatman, MD, MS (dated January 14, 2020)
    b. Exhibit B – List of Materials Reviewed
    c. Exhibit C – Programs Currently Available to Flint Children to Ameliorate the Impact of the Water Crisis

Panagiotis Georgopoulos, PhD

1. Deposition Transcript of Panagiotis Georgopoulos, PhD (dated October 22, 2020)
2. Exhibit 123 – Declaration of Panagiotis (Panos) G. Georgopoulos MS, PhD in Support of Plaintiffs Motion for Class Certification (dated June 27, 2020)
    a. Exhibit 1 – Curriculum Vitae of Panagiotis (Panos) G. Georgopoulos, Dipl.Ing, MS, PhD (dated June 2020)
    b. Exhibit 2 – List of References

Howard Hu, MD

1. Deposition Transcript of Howard Hu, MD – Volume 1 (dated October 12, 2020)
2. Deposition Transcript of Howard Hu, MD – Volume 2 (dated November 5, 2020)
3. Exhibit 81 – Declaration of Howard Hu, MD, MPH, ScD in Support of Plaintiffs Motion for Class Certification (dated June 29, 2020)
    a. Exhibit 1 – Curriculum Vitae of Howard Hu(dated May 2020)
    b. Exhibit 2 – Publications authored by Dr. Hu for previous 10 years
    c. Exhibit 3 – Deposition List Of Howard Hu for 2015-present, as of May 2020)
    d. Exhibit 4 – Consulting Rates for Legal Expert Work for Howard Hu. (dated January 2018)
    e. Exhibit 5 – List of References
4. Various Hu Citation (various dates)
    a. Various Flint Water References (various dates)

Bruce Lanphear, MD

1. Deposition Transcript of Bruce Lanphear MD – Volume 1 (dated September 17, 2020)
2. Deposition Transcript of Bruce Lanphear MD – Volume 2 (dated September 18, 2020)
3. Exhibit 99 – Declaration of Bruce Lanphear, MD, MPH in Support of Plaintiffs Motion for Class Certification (dated June 19, 2020)
    a. Exhibit 1 – Curriculum Vitae of Bruce Perrin Lanphear, MD, MPH
    b. Exhibit 2 – List of References
4. Various Citation
    a. Braun JM, Hoffman E, Schwartz J, Sanchez B, Schnaas L, Mercado-Garcia A, Solano-Gonzalez M, Bellinger DC, Lanphear BP, Hu H, et al. 2012. Assessing

windows of susceptibility to lead-induced cognitive deficits in Mexican children. Neurotoxicology. Oct;33:1040-1047.

b. CDC. 2012. Low Level Lead Exposure Harms Children: A Renewed Call for Primary Prevention. Report of the Advisory Committee on Childhood Lead Poisoning Prevention. Centers for Disease Control and Prevention.
c. Kordas K, Ettinger AS, Bellinger DC, Schnaas L, Tellez Rojo MM, Hernandez-Avila M, Hu H, Wright RO. 2011. A dopamine receptor (DRD2) but not dopamine transporter (DAT1) gene polymorphism is associated with neurocognitive development of Mexican preschool children with lead exposure. J Pediatr. Oct;159:638-643.
d. Min MO, Singer LT, Kirchner HL, Minnes S, Short E, Hussain Z, Nelson S. 2009. Cognitive development and low-level lead exposure in poly-drug exposed children. Neurotoxicol Teratol. Jul-Aug;31:225-231.
e. Schnaas L, Rothenberg SJ, Flores MF, Martinez S, Hernandez C, Osorio E, Velasco SR, Perroni E. 2006. Reduced intellectual development in children with prenatal lead exposure. Environ Health Perspect. May;114:791-797.
f. Taylor CM, Kordas K, Golding J, Emond AM. 2017. Effects of low-level prenatal lead exposure on child IQ at 4 and 8 years in a UK birth cohort study. Neurotoxicology. Sep;62:162-169.

Items Received for Plaintiff Motion for Class Certification

Received July 1, 2020:

1. Class Plaintiffs' Motion for Class Certification (dated June 30, 2020)
2. Memorandum in Support of Class Plaintiffs' Motion for Class Certification (dated June 30, 2020)
3. Declaration of Theodore J. Leopold in Support of Class Plaintiffs' Motion for Class Certification and Appointment of Class Counsel (dated June 30, 2020)
    a. Exhibit 1 – Examining Federal Administration of the Safe Drinking Water Act in Flint, Michigan, Part III: Hearing Before the Committee on Oversight and Government Reform, House of Representatives, One Hundred Fourteenth Congress, Second Session, Serial No. 114-142 (dated March 17, 2016)
    b. Exhibit 2 – Article from the Department of Attorney General, "Schuette Charges Six More in Flint Water Crisis" (dated June 21, 2020)
    c. Exhibit 3 – Letter from Tinka G. Hyde, Director of the U.S. EPA Water Division, to Edward Kurtz, Emergency Manager of the City of Flint, Re: Order for Compliance Pursuant to the Clean Water Act (CWA), 33 U.S.C. §§ 1318 and 1319(a) (dated September 27, 2012)
    d. Exhibit 4 – Email from Michael Alexander, DEQ, to Stephen Busch, DEQ, Re: Flint River Intake Location (dated March 26, 2013)
    e. Exhibit 5 – Michigan Department of Environmental Quality Combined Sewer Overflow (CSO), Sanitary Sewer Overflow (SSO), and Retention Treatment Basin (RTB) Discharge 2013 Annual Report
    f. Exhibit 6 – Analysis of the Flint River as a Permanent Water Supply for the City of Flint (dated July 2011)
    g. Exhibit 7 – Michigan PFAS Action Response Team, Richfield Landfill, Davison, Genesee County (dated February 12, 2020)

h. Exhibit 8 – Diagram of the Richfield Sanitary Landfill (undated)
i. Exhibit 9 – Emails Between Mike Prysby, Jon Bloemker, Stephen Busch, Richard Benzie, and Liane Shekter Smith Re: Flint – Dept of Treasury (dated January 23, 2013)
j. Exhibit 10 – Email from Sara Wurfel to Rick Snyder Re: Genesee Co Water Supply Project Today's Flint Journal (dated October 31, 2012)
k. Exhibit 11 – Letter from Sue F. McCormick, Director of the City of Detroit Water and Sewerage Department, to Inez M. Brown, City Clerk of City of Flint Re: Termination of Contract for the Provision of Water Services by the City of Detroit, Water and Sewerage Department (dated April 17, 2013)
l. Exhibit 12 – Email Calendar Invitation Re. RDS/GT/VB – KWA & DWSD (Water) Meeting (dated April 17, 2013)
m. Exhibit 13 – Emails Between Dayne Walling and Ed Kurtz Re: DWSD (dated April 20, 2013)
n. Exhibit 14 – Letter from Sue McCormick, Director of the City of Detroit Water and Sewerage Department, to Ed Kurtz, Emergency Manager of the City of Flint (dated April 24, 2013)
o. Exhibit 15 – Letter from Edward J. Kurtz, Emergency Manager of the City of Flint, to Kevyn Orr, Emergency Manager of the City of Detroit Re: DWSD Offer Evaluation (dated April 26, 2013)
p. Exhibit 16 – MDEQ Treasury Review Notes (dated March 28, 2013)
q. Exhibit 17 – Excerpts from the Videotaped Deposition of Dayne Walling, Volume II (dated February 21, 2020)
r. Exhibit 18 – Emails Between Dennis Muchmore and Rick Snyder Re: Just a Head's Up (dated April 4, 2013)
s. Exhibit 19 – Emails Between Allison Scott and John Roberts Re: Flint/DWSD (dated April 28 and 29, 2013)
t. Exhibit 20 – Email from Mary Beth Thelen, DEQ, to Stephen Busch, DEQ, Re: City of Flint Drinking Water, Governor's Office Briefing Paper (dated October 1, 2014)
u. Exhibit 21 – Department of Environmental Quality, Governor's Office Briefing Paper, City of Flint Drinking Water Re: Boil Water Advisories (dated October 1, 2014)
v. Exhibit 22 – Emails Between Various City and State Officials Re: Flint Water (dated October 14, 2014)
w. Exhibit 23 – Excepts from the Videotaped Deposition of Stephen Busch, Volume I (dated January 9, 2020)
x. Exhibit 24 – Preliminary Examination, Volume V, in The People of the State of Michigan v. Nicolas Lyon (dated November 1, 2017)
y. Exhibit 25 – Email from Stephen Busch, DEQ, to Richard Benzie, P.E., Kristina Donaldson, DEQ, and Jon Boemker, P.E. Re: Flint Draft Response (dated March 26, 2013)
z. Exhibit 26 – Emails Between Michael Glasgow, City of Flint Water Plant Laboratory and Water Quality Supervisor, and Adam Rosenthal, DEQ, Re: Proposed Water Monitoring – City of Flint (dated April 16 and 17, 2014)
aa. Exhibit 27 – Excerpts from the Videotaped Deposition of Michael B. Glasgow, Volume I (dated February 24, 2020)
bb. Exhibit 28 – Emails Between Various State and Federal Officials Re: High Lead: Flint Water Testing Results (various dates)
cc. Exhibit 29 – Email from Jennifer Crooks to Stephen Busch, DEQ, and Mike Prysby, DEQ, Re: High Lead: Flint Water Testing Results (dated February 26, 2015)
dd. Exhibit 30 – Email from Stephen Busch, DEQ, to Henry James, GCHD, Re: Information Request and Documentation (dated March 10 and 13, 2015)

ee. Exhibit 31 – Emails Between Various State Officials Re: Flint Draft Response (dated March 26 and 27, 2013)
ff. Exhibit 32 – Excerpts from the Rough Draft/Uncertified Transcript of Liane Shekter Smith (undated)
gg. Exhibit 33 – Emails Between Various DEQ and GCHD Officials Re: Information Request and Documentation (dated March 10 and 12, 2015)
hh. Exhibit 34 – Emails Between Various DEQ Officials and Miguel Deltoral and Jennifer Crooks Re: High Lead: Flint Water Testing Results (dated February 26 and 27, 2015)
ii. Exhibit 35 – Emails Between Various DEQ Officials Re: Here's the Interim Report (dated July 9, 2015)
jj. Exhibit 36 – Memorandum from Miguel A. Del Toral, Regulations Manager of the Ground Water and Drinking Water Branch of the U.S. EPA, to Thomas Poy, Chief of the Ground Water and Drinking Water Branch of the U.S. EPA, Re: High Lead Levels in Flint, Michigan – Interim Report (dated June 24, 2015)
kk. Exhibit 37 – Excerpts from the Videotaped Deposition of Adam C. Rosenthal (dated March 5, 2020)
ll. Exhibit 38 – Emails Between Adam Rosenthal, DEQ, and Michael Glasgow, DEQ, Re: Lead/Copper (dated July 9 and 10, 2015)
mm. Exhibit 40 – Emails Between Patrick Cook, DEQ, and Miguel Deltoral Re: Flint Corrosion Control? (various dates)
nn. Exhibit 41 – Email from Jordan Dickinson, Legislative Assistant of Congressman Dan Kildee, Re: Congressman Kildee Letter on Lead in Flint Water (dated September 9, 2015)
oo. Exhibit 42 – Emails Between Various DEQ Officials and Jennifer Crooks, Miguel Deltoral, and LeeAnne Walters Re: High Lead: Flint Water Testing Results (various dates)
pp. Exhibit 43 – Excerpts from the Videotaped Deposition of Bradley J. Wurfel, Volume I (dated May 26, 2020)
qq. Exhibit 44 – Email from Brad Wurfel, DEQ, to Lindsey Smith Re: Dan Wyant's on Record Remarks to the News (dated October 18, 2015)
rr. Exhibit 45 – Emails Between Various City Officials Re: McLaren Bacteria Brief (dated October 3, 2014)
ss. Exhibit 46 – Emails Between Various City and State Officials Re: Flint Water (dated October 14, 2014)
tt. Exhibit 47 – Excerpts from the Videotaped Deposition of Valerie Brader, Volume I (dated April 6, 2020)
uu. Exhibit 48 – Letter from Sue F. McCormick, Director of the City of Detroit Water and Sewerage Department, to Darnell Early, Emergency Manager of the City of Flint, and Dayne Walling, Mayor of the City of Flint, Re: Re-establishing Detroit Water and Sewerage Department Water Service (dated January 12, 2015)
vv. Exhibit 49 – Excerpts from the Oral Deposition of Gerald Ambrose, Volume I (dated June 10, 2020)
ww. Exhibit 50 – Excerpts from the Videotaped Deposition of Daugherty Johnson, Volume I (dated December 17, 2019)
xx. Exhibit 51 – Emails Between Various City Officials Re: Water Plant Upgrades (dated August 15, 2013)
yy. Exhibit 52 – Email from Gerald Ambrose to Dayne Walling Re: All Our Talk and This is the Story☺…Plus Certification of Charter Commission Candidates and Notice that Eric Mays is Considering a Run for Mayor! (dated January 29, 2015)

zz. Exhibit 53 – Press Release Re: Emergency Manager Statement on Water: Spending Extra $12 Million on Detroit Water "Incomprehensible" When Flint Water Just as Safe (dated March 24, 2015)
aaa. Exhibit 54 – Excerpts from the Videotaped Deposition of Howard Croft, Volume I (dated May 28, 2020)
bbb. Exhibit 55 – City of Flint Michigan Contractors, Lockwood, Andrews & Newnam Motor & Repair Services, 13-046 (dated June 26, 2013)
ccc. Exhibit 56 – Profile of Leo A. Daly III, FAIA, RIBA, FRAIA, Chairman and CEO of Lockwood, Andrews & Newnam, Inc. (dated June 20, 2020)
ddd. Exhibit 57 – City of Flint, Flint Water Treatment Plant Rehabilitation – Phase II, Project Work Plan (dated November 22, 2013)
eee. Exhibit 58 – Expert Report of Dr. Larry L. Russell (dated June 30, 2020)
fff. Exhibit 59 – Michigan Department of Environmental Quality, City of Flint Drinking Water Frequently Asked Questions (dated November 24, 2015)
ggg. Exhibit 60 – City of Flint 2014 Annual Water Quality Report
hhh. Exhibit 61 – Operational Evaluation Report, City of Flint, Trihalomethane Formation Concern (dated February 27, 2015)
iii. Exhibit 62 – City of Flint Invitation to Bid for Water Quality Consultant (undated)
jjj. Exhibit 63 – Response to Invitation to Bid, Water Quality Consultant, Proposal No. 15-573 (dated January 29, 2015)
kkk. Exhibit 64 – Resolution to Veolia Water for Water Quality Consultant (dated February 4, 2015)
lll. Exhibit 65 – Excerpts from the Videotaped Deposition of Robert T. Nicholas, Volume I (dated December 9, 2019)
mmm. Exhibit 66 – INTERNAL ONLY: Flint: Key Messages from Veolia (dated February 6, 2015)
nnn. Exhibit 67 – Article from Michigan NPR Radio, "Flint Hires a Water Consulting Firm, UM-Flint Releases Its Own Water Test Results" (dated February 12, 2015)
ooo. Exhibit 68 – Email from Robert Nicholas, Veolia, to Marvin Gnagy and Paul Whitmore, Veolia, Re: Compilation of Notes and Conversations (dated February 12, 2015)
ppp. Exhibit 69 – Emails Between Veolia Staff Re: Flint (dated January 22, 2015)
qqq. Exhibit 70 – Email from Robert Nicholas, Veolia, to James Good and Bruno Valla, Veolia, Re: Flint Background (dated February 13, 2015)
rrr. Exhibit 71 – Emails Between Veolia Staff Re: Flint Proposal Discussion (dated February 2 and 3, 2015)
sss. Exhibit 72 – Handwritten Note Re: Corrosion Control Checking (dated February 18, 2015)
ttt. Exhibit 73 – Spreadsheet with Plant Design and Water Quality Data (undated)
uuu. Exhibit 74 – Excerpts from the Videotaped Deposition of Depin (Theping) Chen, Volume I (dated November 25, 2019)
vvv. Exhibit 75 – Excerpts from the Videotaped Deposition of Marvin Gnagy, Volume I (dated December 12, 2019)
www. Exhibit 76 – Emails Between Veolia Staff Re: Flint (dated February 13, 2015)
xxx. Exhibit 77 – Extracted Text of VWNAOS091608 (undated)
yyy. Exhibit 78 – Emails Between City Officials and Veolia Staff Re: Help with a Flint Journal Article (dated February 9, 2015)
zzz. Exhibit 79 – Emails Between City Officials and Veolia Staff Re: Help with a Flint Journal Article (dated February 9, 2015)
aaaa. Exhibit 80 – Emails Between City Officials and Veolia Staff Re: Help with a Flint Journal Article (dated February 9, 2015)

bbbb. Exhibit 81 – Declaration of Howard Hu, M.D., M.P.H., Sc.D., in Support of Plaintiffs' Motion for Class Certification (dated June 29, 2020)
cccc. Exhibit 82 – Excerpts from the Videotaped Deposition of Rhonda Kelso (dated November 12, 2019)
dddd. Exhibit 83 – Excerpts from the Videotaped Deposition of Barbara Davis (dated November 13, 2019)
eeee. Exhibit 84 – Class Plaintiffs' Proposed Trial Plan (undated)
ffff. Exhibit 85 – Declaration of Pierre Goovaerts, Ph.D., in Support of Plaintiffs' Motion for Class Certification (dated June 27, 2020)
gggg. Exhibit 86 – Expert Report of Robert A. Simons, Ph.D. (dated June 29, 2020)
hhhh. Exhibit 87 – Expert Report of R. Bruce Gamble (dated June 26, 2020)
iiii. Exhibit 90 – Excerpts from the Videotaped Deposition of Darrell Davis (dated November 12, 2019)
jjjj. Exhibit 91 – Excerpts from the Videotaped Deposition of Elnora Carthan (dated January 29, 2020)
kkkk. Exhibit 93 – Excerpts from the Videotaped Deposition of David Munoz (dated December 16, 2019)
llll. Exhibit 94 – Excerpts from the Videotaped Deposition of Tiantha Williams, Volume I (dated December 12, 2019)
mmmm. Exhibit 95 – Plaintiff Francis Gilcreast's Amended Reponses to Defendants' First Set of "Uniform" Interrogatories (dated August 1, 2019)
nnnn. Exhibit 96 – Excerpts from the Videotaped Deposition of Francis L. Gilcreast (dated November 22, 2019)
oooo. Exhibit 97 – Plaintiff Angelo's Coney Island Palace, Inc.'s Amended and Supplemental Response to Defendants' First Set of "Uniform" Interrogatories (dated July 5, 2019)
pppp. Exhibit 98 – Excerpts from the Videotaped Deposition of Neil Helmkay (dated January 9, 2020)
qqqq. Exhibit 99 – Declaration of Bruce P. Lanphear, M.D., M.P.H. in Support of Plaintiffs' Motion for Class Certification (dated June 19, 2020)
rrrr. Exhibit 100 – Flint Water Advisory Task Force Final Report (dated March 2016)
ssss. Exhibit 101 – Email from Robert Nicholas, Veolia, to James Good and Bruno Valla, Veolia, Re: Flint Background (dated February 13, 2015)
tttt. Exhibit 102 – Expert Report of Paolo Gardoni, Ph.D. (dated June 26, 2020)
uuuu. Exhibit 103 – Excerpts from the Videotaped Deposition of Steven T. Luoma (dated June 4, 2020)
vvvv. Exhibit 104 – Excerpts from the Videotaped Deposition of Jeremy Nakashima, Volume I (dated June 22, 2020)
wwww. Exhibit 105 – Excerpts from the Videotaped Deposition of Michael R. Schock, Volume I (dated May 5, 2020)
xxxx. Exhibit 106 – Analysis of the Flint River as a Permanent Water Supply for the City of Flint (dated July 2011)
yyyy. Exhibit 107 – Letter from J. Warren Green, Project Director at Lockwood, Andrews & Newnam, Inc., and Samir F. Matta, Senior Project Manager at Lockwood, Andrews & Newnam, Inc., to Brent Wright, City of Flint Water Treatment Plant Supervisor, Re: Flint Water Treatment Plant Rehabilitation – Phase II (dated June 10, 2013)
zzzz. Exhibit 108 – Veolia Water Quality Report to Emergency Manager Gerry Ambrose (dated March 4, 2014)
aaaaa. Exhibit 109 – Veolia Water Quality Report of Flint, Michigan (dated March 12, 2015)

bbbbb. Exhibit 110 – Email from Robert Nicholas, Veolia, to City Officials Re: Technical Report (dated March 30, 2015)
ccccc. Exhibit 111 – Emails Between Veolia Staff Re: Flint (dated February 13, 2015)
ddddd. Exhibit 112 – Emails Between Veolia Staff Re: Flint (dated February 13, 2015)
eeeee. Exhibit 113 – Emails Between Veolia Staff Re: Internal Only – Confidential Flint Situation (dated February 19, 2015)
fffff. Exhibit 114 – Expert Report of David Keiser, Ph.D. (dated June 28, 2020)
ggggg. Exhibit 115 - Spreadsheet with Water Testing Results from Flint Residences (undated)
hhhhh. Exhibit 116 – Spreadsheet with City of Flint Lead and Copper History Results (undated)
iiiii. Exhibit 117 – Excerpts from the Rough Draft Deposition of Michael Prysby, Volume III (dated June 18, 2020)
jjjjj. Exhibit 118 – Expert Report of David A. Pogorilich (dated June 26, 2020)
kkkkk. Exhibit 119 – Declaration of Daniel P. Keating, PhD in Support of Plaintiffs' Motion for Class Certification (dated June 29, 2020)
lllll. Exhibit 120 – Declaration of Alan Ducatman, MD, MS in Support of Plaintiffs Motion for Class Certification (dated June 28, 2020)
mmmmm. Exhibit 121 – Declaration of Daryn Reicherter, M.D. in Support of Plaintiffs' Motion for Class Certification (dated June 30, 2020)
nnnnn. Exhibit 122 – Declaration of Clifford P. Weisel, M.S., Ph.D., in Support of Plaintiffs' Motion for Class Certification (dated June 28, 2020)
ooooo. Exhibit 123 – Declaration of Panagiotis (Panos) G. Georgopoulos M.S., Ph.D., in Support of Plaintiffs' Motion for Class Certification (dated June 27, 2020)
ppppp. Exhibit 124 – House Oversight and Government Reform Committee Holds Hearing on Flint, Michigan Water Crisis, Part 3 (undated)
qqqqq. Exhibit 125 – Excerpts from the Rough Draft Deposition of Rick Snyder, Volume I (dated June 25, 2020)
rrrrr. Exhibit 126 – Excerpts from the Videotaped Deposition of Dennis Muchmore, Volume II (dated June 9, 2020)
sssss. Exhibit 127 – Letter from Dr. Marc Edwards, Charles P. Lunsford Professor at Virginia Polytechnic Institute and State University, to Elnora Carthan Re: Lead in Water Test Results (dated August 31, 2015)

References Cited by Plaintiff Experts

References Cited by Plaintiff Experts

Borja-Aburto, V. H., Hertz-Picciotto, I., Lopez, M. R., Farias, P., Rios, C., & Blanco, J. (1999). Blood lead levels measured prospectively and risk of spontaneous abortion. *American Journal of Epidemiology*, *150*(6), 590-597.

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